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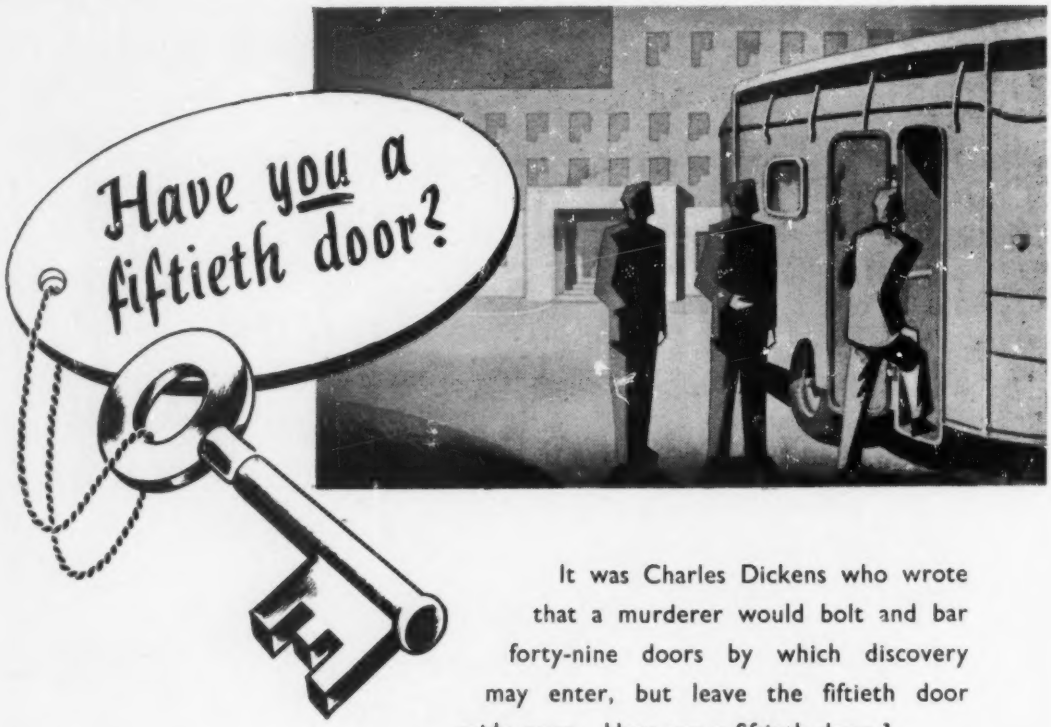

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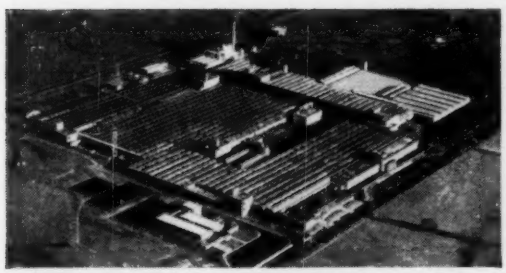

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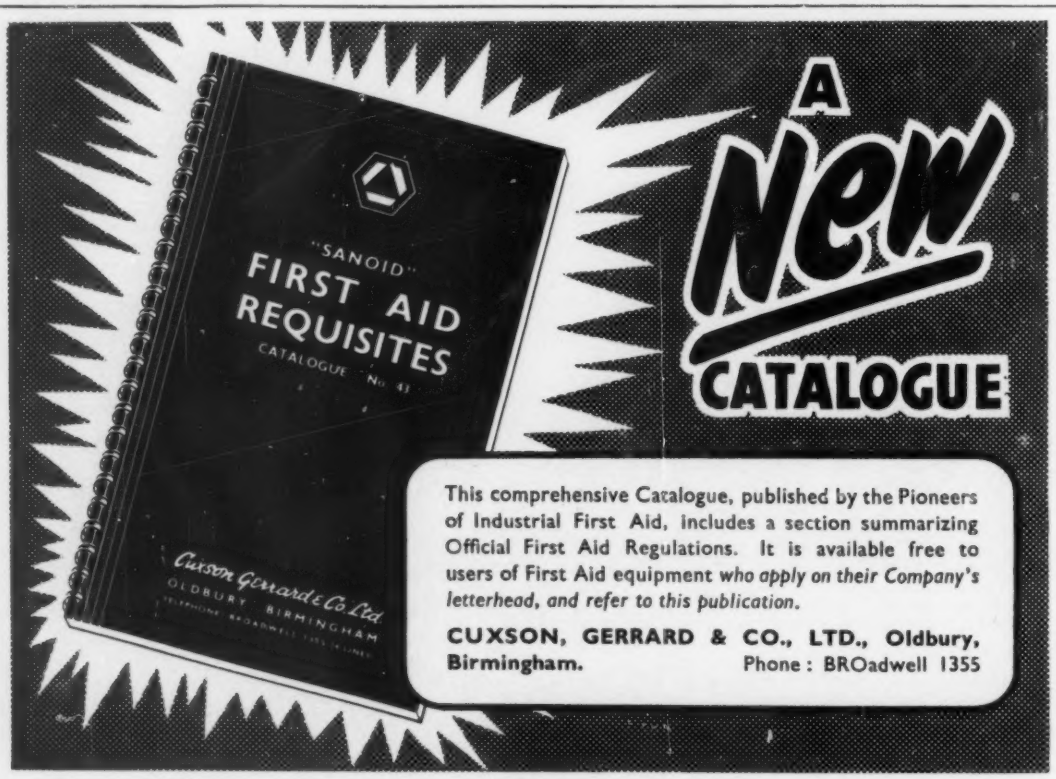
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RESEARCH IN INDUSTRIAL HEALTH IN THE CHEMICAL INDUSTRY *

BY

M. W. GOLDBLATT

From the Imperial Chemical Industries, Ltd., Industrial Hygiene Research Laboratories, Welwyn, Herts

The satisfaction I feel at the opportunity afforded me to add my homage to that of old colleagues who have preceded me in the commemoration of James Mackenzie and his work is of a special kind. Mackenzie was a man with a mission. He also had a vocation, and his life was rich in worth. If James Mackenzie sought to bring what might be called " physical " light to the dark and sick lives of the industrial workers of his time, he brought much spiritual light also. To have enlisted the cooperation of some of the most notable and busy men in public health and medicine through his Industrial Health Education Society required qualities which, when they impinge on other men's minds, raise them to heights they would never wish to leave. These qualities of Mackenzie are those which every medical officer in industry requires.

The workers and staff of an industry are in a real sense the flock of the industrial doctor, and he should be as preoccupied about their physical and mental well-being as the parson is presumed to be about the spiritual life of his flock. His factory is his industrial health education society, but there the people to be taught are not only the workers but the employers also.

Thirty years ago, when James Mackenzie was founding his society, industrial medicine was in the stage of exhortation. The workman was suspicious of the " compo " doctor; the employer might employ a doctor to examine new entrants, for first-aid services, and in compensation cases. Many doctors thus appointed were not permitted to enter the factories at all. The health and well-being of a worker were then of consideration only as they might affect the employer's interests. Then, as now, the appointment of an industrial medical officer and what he was asked to do lay with the employer.

The coming of the second world war gave an impetus to industrial medicine in this country and in many others for which the workers may be thankful. Practitioners now visit factories, join in lectures and discussions, avail themselves of services provided by industry in the factories, and exchange information with the industrial doctor. To-day the stage of exhortation is almost over.

James Mackenzie died in 1944, his society having been wound up at the beginning of the war, but he must have seen the movement towards more and more social realization of responsibility for the health of the nation in a sense more profound than it had ever been. My own satisfaction in paying my tribute to Mackenzie consists in the knowledge that after following with so many of my friends his path in the health education of the worker and his employer I was put in charge of the first industrial hygiene laboratories established by industry in this country, a tangible proof of the awakened realization among industrialists that industrial health is not a question of policy, but one of science, of conscience, and of civility.

Maximum Allowable Concentration of Atmospheric Contaminants in the Working Environment

For an industrial environment where harmful elements, compounds, or radiations are known to be actually or potentially present, it has become customary to prescribe an allowable concentration of dust, gas, fume, or vapour which must not be exceeded if an assurance is sought that men and women may work in that environment without harm. Perhaps more customary in the U.S.A. than in Britain, the term " maximum allowable concentration " (or variants of it) is becoming more familiar here also. It may be recalled that the conception was foreshadowed in this country by Thomas Legge some 45 years ago when he (and Duckering) gave 5 mg./10 cm. as the atmospheric concentration of

* The Mackenzie Industrial Health Lecture delivered in Manchester on July 13, 1954, at the Annual Provincial Meeting of the Association of Industrial Medical Officers.

lead in which engineers and chemists might work. By prescribing a maximum intake of lead, however, there is the implication that the harder a man works in the atmosphere containing lead, the shorter time he should be permitted to do so. Thus, merely to give a maximum permissible concentration without giving the severity of the work and the time engaged per day in such work, leaves one entirely in the dark as to what a man is absorbing. Lane (1949) and Kehoe (1949) substantially agree that at 1·5 to 2 mg./10 cm. " cases of disabling lead intoxication do not occur among men who work regularly in such workrooms, and cases of questionable or mild intoxications are rare ".

But Lane is not slavishly attached to this maximum allowable concentration and insists (*loc. cit.*) that the final test must be the effect on the workmen and, by implication, that mere analysis of the atmosphere is not enough. This statement is of great general significance and may be considered in conjunction with the views of Cook (1945), one of the distinguished workers in the field of maximum allowable concentrations. Cook says :

> " It is to be emphasized that the intent in presenting the maximum allowable concentrations is to provide a handy yardstick to be used as guidance for the routine industrial control of these health hazards—not that compliance with the figures listed would guarantee protection against ill-health on the part of exposed workers, nor should the maintenance of the suggested concentrations be considered a substitute for medical control."

The use of the words " suggested concentration " is a sufficient indication that the conception is not precise.

Drinker and Cook (1949) in a later contribution emphasized, by implication, the imprecise nature of these concentrations when they proposed a zoning system, whereby, it was stated, the toxicity of an industrial atmospheric contaminant could be quickly assessed from the zone in which it falls. Six zones were given as follows :—

500–2,000 p.p.m.	acetone, petrol, ether
100– 500 p.p.m.	methanol, toluene
20– 100 p.p.m.	benzene, butanol, CCl_4, CO
2– 20 p.p.m.	H_2S, CS_2, $C_2H_3Cl_3$, HCl, HCN
0·1– 2 p.p.m.	Cl, $COCl_2$, AsH_3, $(CH_3)_2SO_4$
0·1 p.p.m.	radon, radioactive gases, etc.

They added : " The zoning scheme is for the classification of information and not for the justification of excessive exposure or misguided legal interpretation."

Tables of maximum allowable concentrations must not evoke responses which are entirely unjustified and even dangerous. Classification in zones cannot fail to influence non-medical personnel by suggesting similar toxicities of substances, the effects of which are entirely different. For a doctor the association of a hazard with a value or a zone of values is desirable to supplement the picture already in his mind of one or more features of the effects of the compounds. Non-medical personnel, however, are not as a rule in the same position. They are likely to use, and in fact do use, phrases such as " Arsine—oh yes, about as toxic as bromine, isn't it ? ", or, " Tetrachloroethane—yes, yes, quite troublesome—about as bad as hydrochloric acid ", because, in fact, their maximum allowable concentration values are identical, but, it must be noted, for very different reasons. Toxic hazards should, in general, be considered as identities with their own numerical data attached to them and their own effects attached to the numerical data.

Hazards may have to be classified into groups for convenience or as aids to memory, but this must be on the basis of similarity of toxic effects and not on the fortuitous closeness of maximum allowable concentrations.

The fact that both HCl and HCN are in the same Drinker and Cook zone (2–20 p.p.m.) as aniline, acetic acid, and acrylonitrile tells us nothing of their effects or relative dangers. This is even more strongly illustrated in the highly dangerous zone 0·1–2 p.p.m.

DRINKER AND COOK ZONES (EXPANDED)

0·1 p.p.m.	0·5 p.p.m.	1·0 p.p.m.	2·0 p.p.m.
Hydrogen selenide	Arsine	Chlorine	*p*-Chlor aniline
Iodine	Bromine	Hydrazoic acid	*p*-Chlor-nitrobenzene
Stibine	Cyanogen chloride		Ethylene chlorohydrin
	Ethyleneglycol dinitrate		Hydrogen fluoride
	Phosgene		
	Phosphorus trichloride		
	Ketene		
	Nitroglycerine		

N.B.—HCN 10 p.p.m.

In this table we have some of the most fulminating poisons met with in industry, and it would be in the highest degree undesirable to bracket them together in any sense whatever. For, whereas some of the limits set are those for immediate irritation, others are for delayed effects, and others again for cumulative effects. Some appear because of their effects on the circulatory mechanics ; others because of the effects of their metabolic products on haemoglobin ; still others because they cause a dangerous increase of the permeability of the pulmonary vessels ; and others because of disruptive effects on the envelope of the blood corpuscles.

So diverse a picture demands different degrees of urgency in persons whose responsibility it is to prevent concentrations above those prescribed. Moreover, the sense of urgency must clearly depend

also on the physical properties of the compounds involved. Everyone concerned must be made conscious of clinical urgency as well as of quantitative urgency. The state of mind which informs our own approach to environmental contaminants is that implied in the table of concentrations issued from my laboratories (Table 1).

The actual values given may require modification in the light of experience, but as each figure has emerged from a searching examination of clinical and experimental records, great modifications are not likely. Still, some have already been made ; for example, in the case of formaldehyde, acetone, ammonia, ethanol.

The first three columns indicate the times required by certain concentrations to produce very severe and dangerous symptoms ; the next two columns give concentrations which are not tolerated ; the last two columns give concentrations which set an upper limit to satisfactory conditions in respect of the particular substance (design concentrations).

The use of the words " maximum allowable concentration " has been avoided because at I.C.I. we hold that no concentration is allowable. Some are worse than others but all are bad.

Animal Experiment

For industrial toxicological purposes it is important to use animals in experiments simulating industrial conditions. Most industrial poisonings are the result of absorption by inhalation or by the skin, much more rarely by ingestion and by the eyes, and most, acute and chronic, are to mixtures of substances. Very little is known of the adjuvant effects of one substance thus absorbed on the toxic effects of others.

Factors of safety must be assumed if results of animal experiments are applied to man, factors depending upon man's greater susceptibility and upon his greater activity during work. If an estimate can be made of the amount of a toxic substance daily absorbed by men at work, the acceptability of the environmental conditions in which it occurs can be estimated by exposing animals to multiples of that estimate. Since the metabolism of small animals is many times greater than that of man, gas, vapour, or fume concentrations at which animals can subsist without adverse effects may be reasonably regarded as equally inoffensive to man as far as overt signs are concerned.

Cutaneous absorption of toxic materials is of great importance in the organic chemical industry and in the field use of toxic insecticides, fungicides, and herbicides.

Quantitative measurement of the degree of cutaneous absorption in animals is difficult, but comparative measurements can be made with small animals by time measurements from the onset of symptoms to death, or to measurable biochemical effects after immersion of anatomical appendages, such as paws or tails, in known concentrations of the compounds studied. Many substances are more toxic cutaneously than orally.

The demonstration of dermatitic effects in animals which do not perspire in any sense similar to that seen in man is usually impossible although an urticaria-like reaction is sometimes seen. The phenomena of " contact dermatitis ", " sensitization dermatitis ", " allergic dermatitis ", or " eczema " are not reproducible in animals in experimental conditions. Complicated immunological demonstrations that some chemical compounds can act in appropriate conditions as skin allergens are possible and such demonstrations have corresponded with the known properties of some organic compounds. Erythema and oedema should be measured according to determined scales (Draize, Woodard, and Calvery, 1944). The skin of laboratory animals does not respond as does human skin to the host of chemical substances which induce dermatitis of the acute variety so frequently seen in industrial conditions. In the case of cutaneous cancer the correspondence is closer. Thus, animal experiment is largely directed to finding whether given chemical compounds induce direct irritant effects on the skin.

Physiological effects (on the circulation, respiration, blood pigments, tissue and blood enzymes, renal and hepatic function, growth, fertility, central nervous system), in the sense of reversible effects, can be demonstrated by animal experiment with relative ease, and the results in some cases applied to the clinical control of hazards in the factory. Contact dermatitis in man disappears on removal from exposure, but the effect is not truly reversible.

A fall in blood pressure, readily demonstrable in animals, is used by some American authorities as a clinical-statistical index of undue absorption of many toxic organic compounds. There are some explosive compounds (made and used both here and in other countries) which are rapidly hypotensive in working conditions : blood pressure determinations are essential for proper medical control in these cases, especially as pseudo-anginal attacks may follow long-term exposure. Many industrial compounds can be shown experimentally to depress the heart, dilate the peripheral vessels, or increase vascular permeability. Others, by cholinesterase inhibition, lead to parasympathetic stimulation and vagal effects on the heart. The question of the establishment of hypertension, perhaps of renal origin, in chronic lead absorption is not resolved.

TABLE 1

TOXIC CONCENTRATIONS OF VARIOUS GASES, DUSTS, FUMES, AND METALS IN THE ATMOSPHERE

(I.C.I. Industrial Products and Health Research Committee)

No.	Gas	(1) Concentrations Causing Severe Toxic Effects in Persons Exposed for the Stated Times			(2) Concentrations which, if Exposure Continues for more than a Short Time, may Lead to Symptoms of Illness		(3) *Concentrations in General Atmosphere of Plant Greater than those below Indicate Unsatisfactory Conditions*	
		(p.p.m. v/v)	(mg./cu.* metre 20°C.)	Time of Exposure (Min.)	(p.p.m. v/v)	(mg./cu.* metre 20°C.)	*(p.p.m. v/v)*	*(mg./cu.* metre 20°C.)*
1	Acetaldehyde	1,000	1,830	60	500	915	*200*	*366*
2	Acetic acid	200	500	60	40	100	*20*	*50*
3	Acetone	4,000	9,650	60	800	1,930	*400*	*965*
4	Acetone cyanohydrin	40	140	1	20	70	*10*	*35*
5	Acetonyl acetone	300	1,424	60	150	712	*75*	*356*
6	Acetophenone	80	400	60	40	200	*20*	*100*
7	Acetyl chloride	10	33	1	2	6·6	*1*	*3·3*
8	Acrolein	20	46	1	8	18·6	*5*	*11·6*
9	Acrylonitrile	100	220	1	50	110	*20*	*44*
10	Allyl alcohol	40	96	1	20	48	*5*	*12*
11	Allyl chloride	200	636	60	100	318	*50*	*159*
12	Ammonia	500	355	1	200	142	*100*	*71*
13	*iso* Amyl acetate	1,000	5,410	60	300	1,623	*100*	*541*
14	*iso* Amyl alcohol	400	1,464	60	200	732	*100*	*366*
15	Aniline	80	312	60	20	78	*10*	*39*
16	Arcton 6 (Freon 12) (Difluorodichloromethane)	50,000	251,700	60	20,000	100,680	*10,000*	*50,340*
17	Arsine	10	32	1	1	3·2	*0·5*	*1·6*
18	Benzene (Benzol)	1,500	4,800	60	500	1,600	*50*	*160*
19	Benzine (as Hexane)	3,000	10,728	60	1,000	3,576	*250*	*894*
20	Benzyl acetate	100	616	60	50	313	*15*	*94*
21	Benzyl chloride	20	100	1	10	50	*5*	*25*
22	Bromine	3	20	1	1	6·6	*0·5*	*3·3*
23	Butadiene	8,000	17,968	60	5,000	11,230	*2,500*	*5,615*
24	*n*-Butanol (Butyl alcohol)	1,000	3,080	60	100	308	*50*	*154*
—	2-Butanone (Methyl ethyl ketone)	See No. 90 Methyl ethyl ketone						
25	*n*-Butyl acetate	2,000	9,650	60	500	2,412	*200*	*965*
26	*n*-Butyl methacrylate	800	4,724	60	400	2,362	*200*	*1,181*
27	Carbon dioxide	30,000	54,930	60	10,000	18,310	*5,000*	*9,155*
28	Carbon disulphide	500	1,600	60	150	480	*10*	*32*
29	Carbon monoxide	400	464	60	100	116	*50*	*58*
30	Carbon tetrachloride	2,000	12,800	60	500	3,200	*50*	*320*
31	*p*-Chloraniline	8	44	1	4	22	*2*	*11*
32	(*mono*) Chlorobenzene	400	1,872	60	200	936	*75*	*351*
33	2-Chlorobutadiene	100	368	1	50	184	*25*	*92*
34	Chlorine	10	29	1	4	12	*1*	*2·9*
35	*p*-Chloronitrobenzene	10	66	1	4	26	*1*	*6·6*
36	Chloroform	2,000	9,960	60	500	2,490	*50*	*249*
37	(*o* & *p*) (*mono*) Chlorotoluene	400	2,106	60	200	1,053	*75*	*395*
38	Cyanogen chloride	5	13	1	2	5·2	*0·5*	*1·3*
39	Cyclohexane	2,000	6,990	60	800	2,796	*400*	*1,398*
40	Cyclohexanol	1,000	4,160	60	400	1,664	*100*	*416*
41	Cyclohexanone	1,000	4,080	60	200	816	*75*	*306*
42	Cyclohexylamine	100	410	1	40	164	*20*	*82*
43	*o*-Dichlorobenzene	300	1,836	60	100	612	*25*	*153*
44	ββ'Dichlorodiethyl ether	100	593	1	30	178	*15*	*89*
45	(*cis* & *trans*) Dichloroethylene	2,000	8,072	60	1,000	4,036	*500*	*2,018*
46	Dicyclohexylamine	50	388	60	40	302	*20*	*151*
47	Diethyl carbonate	800	3,928	60	400	1,964	*200*	*982*
48	Di-isobutylene	4,000	18,640	60	2,000	9,320	*1,000*	*4,660*
49	Di-isobutyl ketone	400	1,896	60	200	948	*100*	*474*
50	Dimethyl dioxane	500	2,412	60	300	1,447	*200*	*965*
51	Dimethyl sulphate	15	78	1	10	52	*5*	*26*
52	Dioxane	500	1,830	60	300	1,098	*200*	*732*
53	Ethanol (Ethyl alcohol)	8,000	15,312	60	2,000	3,828	*1,000*	*1,914*
54	Ether (diEthyl)	8,000	24,624	60	2,000	6,156	*500*	*1,539*
55	β-Ethoxyethyl methacrylate	500	3,285	60	200	1,314	*100*	*657*
56	Ethyl acetate	2,000	7,320	60	800	2,928	*400*	*1,464*
57	Ethyl acetoacetate	200	1,080	60	100	540	*50*	*270*
58	Ethyl benzoate	200	1,248	60	100	624	*50*	*312*
59	Ethyl bromide	250	1,135	60	100	454	*50*	*227*
60	Ethyl chloride	10,000	26,830	60	5,000	13,415	*2,000*	*5,366*
61	Ethylene chlorhydrin	20	68	60	10	34	*2*	*7*
62	Ethylene dichloride	500	2,050	60	100	410	*50*	*205*
63	Ethylene glycol dinitrate	20	128	60	1	6·4	*0·5*	*3·2*

Concentrations shown in italic are tentative and are issued as a guide. Figures in all columns will be subject to review as more data become available.

* 1 mg./cu. metre ≡ 4·37 × 10^{-4} grains/cu. ft.

Continued

Table 1 continued

No.	Gas	(1) Concentrations Causing Severe Toxic Effects in Persons Exposed for the Stated Times			(2) Concentrations, which, if Exposure Continues for more than a Short Time, may Lead to Symptoms of Illness		(3) *Concentrations in General Atmosphere of Plant Greater than those below Indicate Unsatisfactory Conditions*	
		(p.p.m. v/v)	(mg./cu.* metre 20°C.)	Time of Exposure (Min.)	(p.p.m v/v)	(mg./cu.* metre 20°C.)	*(p.p.m. v/v)*	*(mcg./u.* metre 20°C.)*
64	Ethylene oxide	250	450	60	100	180	*10*	*18*
65	Ethyl formate	1,000	3,080	60	400	1,232	*200*	*616*
66	Ethylidene dichloride	400	1,648	60	200	824	*50*	*206*
67	Ethyl silicate	400	3,464	60	200	1,732	*100*	*866*
68	Formaldehyde	100	120	1	30	36	*10*	*12*
—	Freon 12 (Arcton 6)	See No. 16 Arcton 6.						
69	Hydrazoic acid	10	18	60	4	7·2	*1*	*1·8*
70	Hydrogen chloride	50	75	1	20	30	*10*	*15*
71	Hydrogen cyanide	40	44	1	20	22	*10*	*11*
72	Hydrogen fluoride	40	34	1	10	8·5	*2*	*1·7*
73	Hydrogen selenide	2	6	1	0·5	1·5	*0·1*	*0·3*
74	Hydrogen sulphide	200	280	1	50	70	*20*	*28*
75	Iodine	0·5	5·5	1	0·2	2·2	*0·1*	*1·1*
76	Isophorone	40	228	60	20	114	*10*	*57*
77	Ketene	2	3·6	1	1	1·8	*0·5*	*0·9*
78	Lauryl mercaptan	20	168	1	10	84	*5*	*42*
79	Mesityl oxide	200	816	1	100	408	*50*	*204*
80	Methacrolein	10	29	1	5	15	*2*	*5·8*
81	Methacrylic acid	1,000	3,575	1	400	1,430	*200*	*715*
82	Methallyl alcohol	150	450	1	100	300	*50*	*150*
83	Methanol (Methyl alcohol)	2,000	2,560	60	500	640	*200*	*256*
84	Methyl acetate	500	1,540	60	200	616	*100*	*308*
85	Methyl acrylate	100	356	1	50	178	*25*	*89*
86	Methyl bromide	250	1,000	1	50	200	*20*	*80*
87	Methyl *iso*-butyl ketone	1,000	4,160	60	400	1,664	*200*	*832*
88	Methyl α-chloracrylate	4	20	1	2	10	*1*	*5*
89	Methyl chloride	1,500	3,150	60	500	1,050	*100*	*210*
90	Methyl ethyl ketone (2-Butanone)	2,000	5,990	60	500	1,498	*200*	*599*
91	Methyl iodide	40	236	1	20	118	*10*	*59*
92	Methyl cyclohexanone	300	1,400	60	150	700	*75*	*350*
93	Methylene chloride	2,000	7,072	60	1,000	3,536	*500*	*1,768*
94	Methyl formate	1,000	2,495	60	400	998	*200*	*499*
95	Methyl methacrylate	3,000	12,480	60	2,000	8,320	*1,000*	*4,160*
96	Naphtha distillate (as Cumene)	300	1,500	60	150	750	*50*	*250*
97	Nickel carbonyl	4	28	1	2	14	*1*	*7*
98	Nitrobenzene	200	1,020	60	40	204	*1*	*5·1*
99	Nitroethane	800	2,496	60	500	1,560	*200*	*624*
100	Nitrous fumes (as NO_2)	100	190	1	30	57	*10*	*19*
101	Nitroglycerine	20	189	60	1	9·4	*0·5*	*4·7*
102	Nitromethane	800	2,028	60	500	1,268	*200*	*507*
103	1-Nitropropane	400	1,480	60	200	740	*100*	*370*
104	2-Nitropropane	400	1,480	60	200	740	*100*	*370*
105	*o*-Nitrotoluene	200	1,140	60	40	228	*1*	*5·7*
106	Perchloroethylene (Tetrachloroethylene)	1,000	6,905	60	400	2,762	*200*	*1,381*
107	β-Propiolactone	100	300	1	20	60	*10*	*30*
108	*iso*-Propyl alcohol	2,000	4,995	60	800	1,998	*400*	*999*
109	Phosgene	5	21	1	1	4·2	*0·5*	*2·1*
110	Phosphorus trichloride	2	12	1	1	5·8	*0·5*	*2·9*
111	Stibine	0·5	2·5	1	0·2	1	*0·1*	*0·5*
112	Styrene	1,000	4,330	60	200	866	*100*	*433*
113	Sulphur dioxide	200	520	1	20	52	*10*	*26*
114	Sulphur monochloride (S_2Cl_2)	20	112	1	10	56	*5*	*28*
115	Sulphuryl chloride	10	56	1	4	22	*1*	*5·6*
116	Tetrachlorethane	50	350	60	20	140	*10*	*70*
—	Tetrachloroethylene (Perchloroethylene)	See No. 106 Perchloroethylene.						
117	Thionyl chloride	20	100	1	10	50	*5*	*25*
118	Thiophosphoryl trichloride	10	70	1	4	28	*1*	*7*
119	Trichloroethylene	2,000	10,940	60	800	4,376	*400*	*2,188*
120	Toluene (Toluol)	1,000	3,830	60	300	1,149	*100*	*383*
121	(*o*, *m*, & *p*) Toluidines	40	176	60	10	44	*5*	*22*
122	Vinyl chloride	3,000	7,800	60	1,500	3,900	*500*	*1,300*
123	Xylenes (Xylols)	1,000	4,410	60	300	1,323	*100*	*441*
124	Xylidines	40	200	60	10	50	*5*	*25*
	Dusts, Fumes, and Metals							
125	Antimony (dust or salts) (as Sb)	—	—	—	—	—	—	*0·5*
126	Arsenious oxide	—	—	—	—	—	—	*0·5*
127	Barium salts (as Ba)	—	—	—	—	—	—	*0·5*

Concentrations shown in italic are tentative and are issued as a guide. Figures in all columns will be subject to review as more data become available.

* 1 mg./cu. metre ≡ 4·37 × 10^{-4} grains/cu. ft.

Continued

Table 1 continued

No.	Gas	(1) Concentrations Causing Severe Toxic Effects in Persons Exposed for the Stated Times			(2) Concentrations which, if Exposure Continues for more than a Short Time, may Lead to Symptoms of Illness		(3) *Concentrations in General Atmosphere of Plant Greater than those below Indicate Unsatisfactory Conditions*	
		(p.p.m. v/v)	(mg./cu.* metre 20°C.)	Time of Exposure (Min.)	(p.p.m. v/v)	(mg./cu.* metre 20°C.)	(p.p.m. v/v)	(mg./cu.* metre 20°C.)
128	Benzidine	—	—	—	—	—	—	*0·015*
129	Cadmium	—	—	—	—	—	—	*0·1*
130	Chlorinated diphenyl	—	—	—	—	—	—	*1*
131	Chlorinated naphthalenes	—	—	—	—	—	—	*1*
132	Chromates (as CrO_3)	—	—	—	—	—	—	*0·1*
133	Dinitrocresol (and salts)	—	—	—	—	—	—	*0·5*
134	Dinitrophenol (and salts)	—	—	—	—	—	—	*1*
135	Dinitroresorcinol	—	—	—	—	—	—	*1*
136	Dinitrotoluene	—	—	—	—	—	—	*1·5*
137	"Dowthern A"	—	—	—	—	—	—	*2*
138	Lead (and salts)	—	—	—	—	—	—	*0·15*
139	Mercury	—	—	—	—	—	—	*0·1*
140	α-Naphthylamine	—	—	—	—	—	—	*0·01*
141	β-Naphthylamine	—	—	—	—	—	—	*0·01*
142	"Parathion"	—	—	—	—	—	—	*1*
143	Pentachlorphenol	—	—	—	—	—	—	*0·5*
144	*p*-Phenylene diamine	—	—	—	—	—	—	*0·1*
145	Phosphorus pentachloride	—	—	—	—	—	—	*1*
146	Potassium permanganate	—	—	—	—	—	—	*5*
147	Sulphuric acid	—	—	—	—	—	—	*1*
148	Sodium cyanide	—	—	—	—	—	—	*5*
149	Tetryl	—	—	—	—	—	—	*1·5*
150	T.N.T.	—	—	—	—	—	—	*2*
151	Zinc oxide	—	—	—	—	—	—	*10*

Concentrations shown in italic are tentative and are issued as a guide. Figures in all columns will be subject to review as more data become available.

*1 mg./cu. metre ≡ $4{\cdot}37 \times 10^{-4}$ grains/cu. ft.

Changes in respiration and the respiratory system are usually secondary to irritation of the respiratory tract, to changes in blood pigment, to central depression, and to direct damage of the alveolar network. Less direct effects are produced by cholinesterase inhibitors, which lead to powerful parasympathetic stimulation, and by inhibitors of oxidative enzymes. The asthma-like attacks induced by some aromatic diamines and di-isocyanates are reversible.

It is unusual for the lungs to be the seat of transformation of compounds. But in the case of ethylene oxide, which has a wide application in the present-day chemical industry and in the fumigation of food, combination with water in the lung can yield toxic glycols which may easily have long-term effects.

Delayed effects on the lung itself (oedema, haemorrhage, emphysema) can be foreseen by animal experiment. Recent investigation in my laboratories of the notorious "nitrous fumes", which have been responsible for many deaths from pulmonary oedema, shows that the potent agent is N_2O_5 and that N_2O_4 is much less toxic as is also nitric acid vapour (Diggle and Gage, 1954).

Any toxic dust is injurious to the lungs although the pneumoconioses, and in particular silicosis, are our most serious and extensive industrial pulmonary diseases.

Fig. 1 shows a section of a lung of a rat which, with a group of other rats, was exposed for eight hours a day for many months to an atmosphere of 2 mg./cm. K_2CrO_4 as a very fine dust. The animals were well enough: there was a period of coughing and harsh breathing, but nothing serious. They lived on in quietude and sustained the chromate with bored fortitude but the lung shows large and small areas of exsanguinated alveoli crammed with loaded histiocytes in various stages of degeneration. Functionally these areas are out of action. The cell debris in the alveoli contributes further to loss of function until disposed of. Dilated respiratory bronchioles and some emphysema, due partly to the injurious effect of the chromate on the alveolar septa, and partly as compensation to the loaded alveoli, are also seen.

Fig. 2 is a high-power picture of a portion of a guinea-pig's lung after exposure for months to a very high concentration of lead acetate (40–50 mg./cm.). The origin of the dust cells from the alveolar septal cells is clearly seen, but monocytic cells undergoing hypertrophy from the capillary blood appear also to be passing into the alveoli.

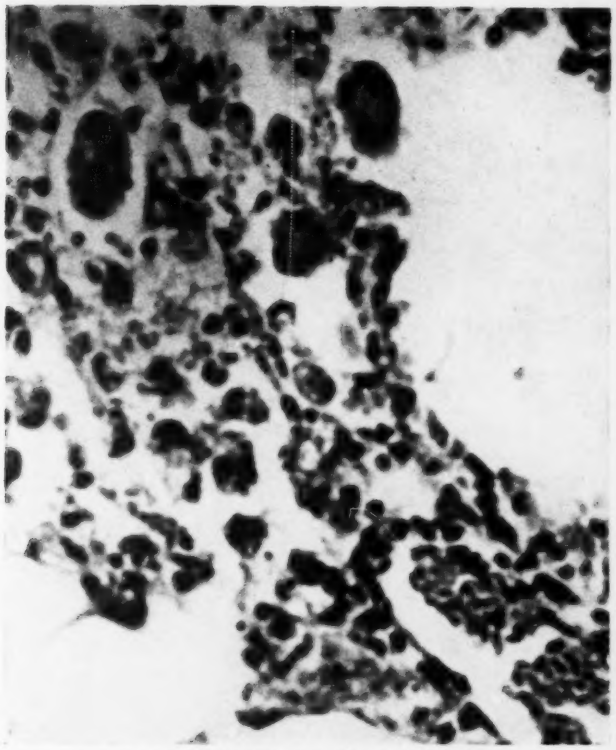


FIG. 2.—Guinea-pig lung after chronic inhalation of fine lead acetate dust—origin of mononuclear phagocytes from blood and alveolar walls. Active phagocytosis seen both in the wall and in the lumen of the alveoli and coarse granular pigmented material in the phagocytes. × 300.

FIG. 1.—Rat lung after chronic exposure to fine potassium chromate dust; many areas of exsanguinated, functionless alveoli filled with histiocytic phagocytes and many ruptured alveoli. × 100.

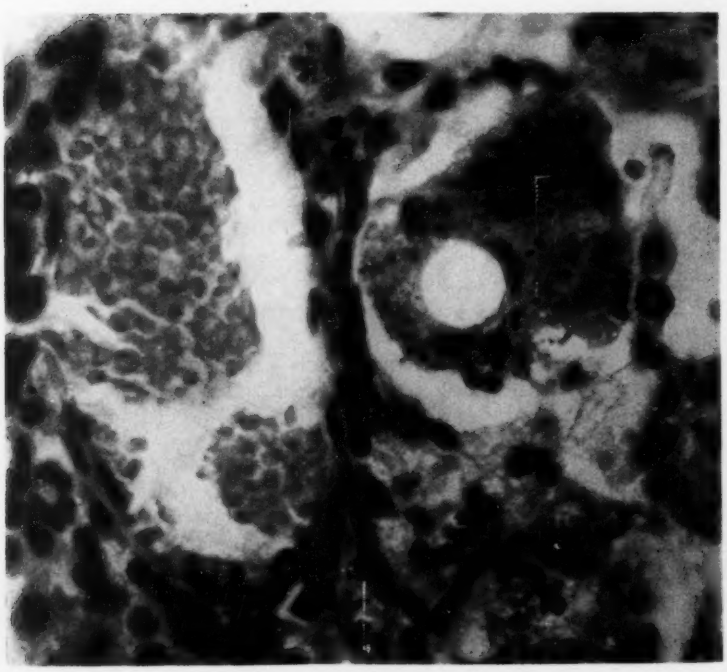


FIG. 2a.—Phagocytosis of blood phagocytes by macrophages deriving from septal cells; details of coarse pigment granules in guinea-pig lung. × 1200.

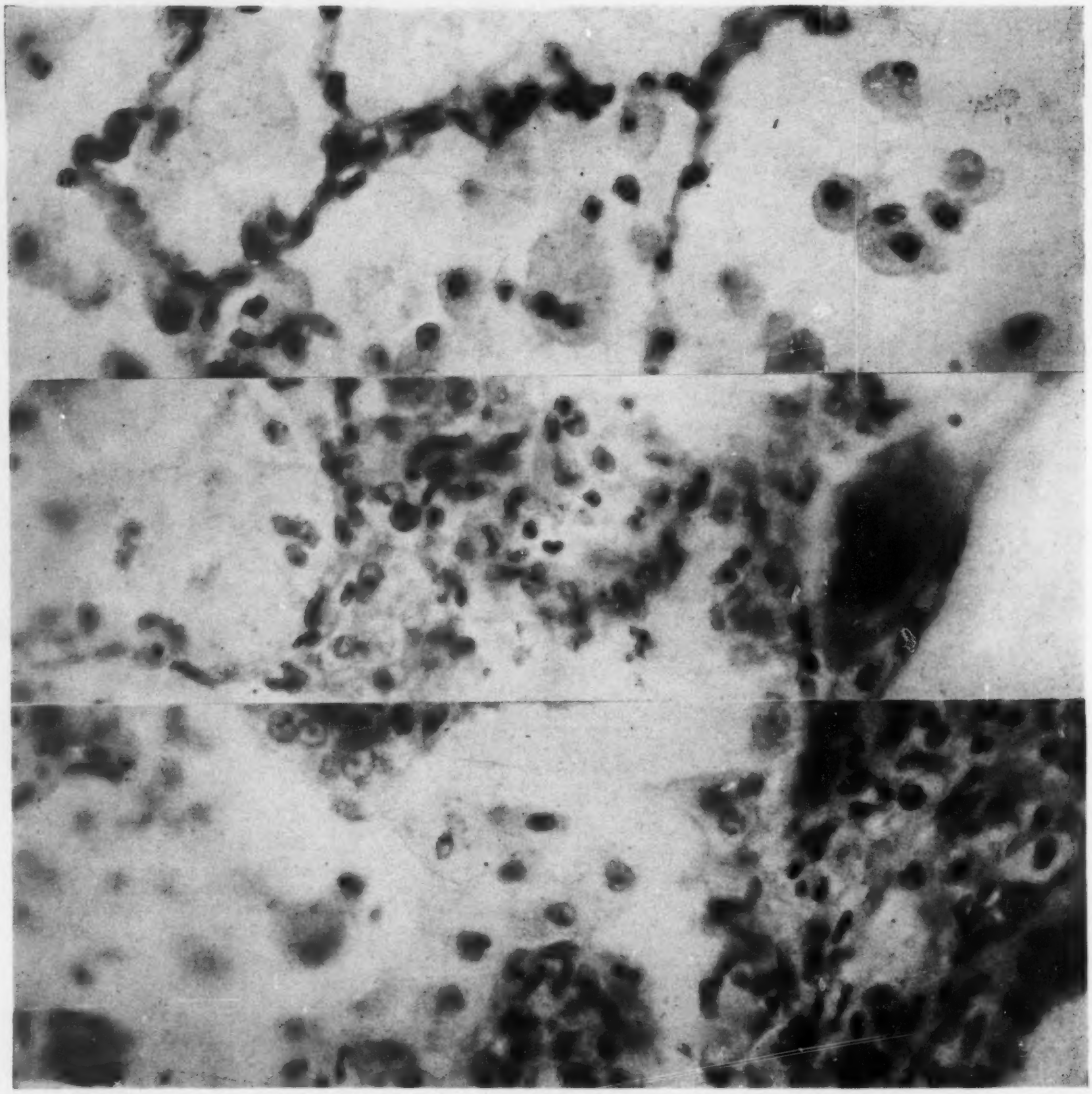


FIG. 3.—Rabbit lung showing chronic inhalation of fine lead acetate dust. Three areas of same lung showing different stages in development and death of lung phagocytes; small alveolus crammed with dead and dying phagocytes swollen with absorbed particles; note multinuclear macrophage. × 560.

These cells are later engulfed by the macrophages developed from the septal cells after having acted as dust cells themselves. The macrophages are seen to contain dark pigmented granules and nuclei in various stages of degeneration (Fig. 2a). In Fig. 2a the extent of phagocytic activity is striking. In Fig. 3 we see the progressive changes from the well stained cell in the alveolar wall to the dead dust cells in the alveolar spaces.

The effectiveness of the lung barrier to a toxic dust must depend upon the availability of phagocytes to act as a brake on absorption. At so high a concentration as that used in these experiments blood cells evidently enter as an additional defence. The barrier to dusts presented by the lung is paid for in the case of toxic dusts by a denudation of the precursors of the so-called dust cells (*i.e.* modified septal cells) and in oxygen capacity by the occupation of alveolar spaces by highly charged cells and cell debris when the toxic material is discharged. The formation of giant multinucleate cells also occurs in the chronic inhalation of toxic dust (Fig. 3). In a universe of dust processes of this kind are inevitable but it is our business to combat industrial dust with other weapons than our lungs.

Changes in blood pigments are mainly found in industry among those exposed to carbon monoxide, various aromatic nitro- and amino-compounds, and

metallic elements which interfere with haemoglobin formation. These effects cannot all be demonstrated with equal ease in all species of laboratory animals.

The deliberate induction of methaemoglobinaemia in the treatment of cyanide poisoning is of practical importance, and recovery in very severe cases has been obtained by Lloyd Potter (1950). The method depends upon the intravenous injection of sodium nitrite which, by forming methaemoglobin, permits the circulating cyanide to react to form the much less toxic cyanmethaemoglobin and upon the intravenous injection of sodium thiosulphate which accelerates the formation of thiocyanate from the now slowly liberated cyanide.

Renal and hepatic function can be affected by many chemical agents ; among these are certain industrial metallic poisons, organic solvents, notably chlorinated aliphatic hydrocarbons, explosives, derivatives of glycols. Reversibility in these cases is endangered for the change-over from dysfunction to structural breakdown is poised precariously. The peculiar position of trichloroethylene among the commonly used solvents, however, indicates how subtle must be the mechanism which determines its low toxicity, which is perhaps related to its ready metabolism to the non-toxic trichloroacetic acid (Taylor, 1936 ; Powell, 1945).

For certain metabolic aspects of toxicity and carcinogenicity the use of isotopes is assuming wider and wider significance. A bladder carcinogen with one carbon C^{14} has recently been prepared by members of my department in collaboration with Amersham (Henson, 1953 ; Catch, Huggill, and Somerville, 1953). We have already been able to establish important metabolic pathways and the long retention of compounds carrying the labelled atom in the body (Henson, Somerville, Farquharson, and Goldblatt, 1954). The detection of the location of toxic compounds in cells by autoradioactivity in histological sections is already a developing method.

The ultimate fate of most materials absorbed in industrial conditions is unknown. A great deal is known about some of the final forms in which many chemical substances are disposed of in animals, but we are very rarely able to strike a balance by ordinary or even extraordinary chemical means. The subtle ways in which complex substances introduced into the body in large part " disappear " raise many difficulties and apprehensions. Nevertheless, by using labelled compounds a new era has been opened in obtaining almost complete balance between intake and output of substances containing isotopic atoms, and in discovering how long such substances or their derivatives are retained in the body. In addition it is possible to track them through the various routes they can take in the body and, if retained for long periods, to learn where they are deposited.

Industrial metabolic poisons interfering with phosphorylating processes are dinitroorthocresol (D.N.O.C.), dinitrophenol (D.N.P.), and pentachlorphenol, the former two being responsible for both clinical and industrial deaths, and the latter for recent industrial deaths. Dinitro aromatic compounds require careful study as some may induce cataract. Indirect metabolic effects may arise from interference with normal thyroid function as in the case of some alkyl-nitro-amino derivatives of phenol.

The haematopoietic system is one of the first examined in the case of most industrial chemical hazards with chronic effects. Blood counts are sometimes undertaken on workers in many different branches of the chemical industry, especially where hydrocarbon and chlorinated hydrocarbon solvents, explosives, some metals, radioactive materials, and many other materials are made or used. Animal experiment often gives the appropriate lead as to the nature of the attack on the blood-forming organs or on the blood itself, although there are difficulties from the much greater variability of the blood picture in animals than in man. Reversibility of effects on the blood depends upon removal of the noxa and on the functional recovery of the bone marrow.

Clinical and Experimental Aspects of Lead Intoxication

Much has been done to elucidate the clinical picture and pathological processes of lead intoxication and poisoning. As the result of 12 years' experience of men in a factory where lead acetate, lead pigments, and paints were manufactured certain clinical and elementary propositions have been formulated. The first is that the control of the health of workers exposed to any lead hazard is easy and effective by routine determination of (*a*) haemoglobin, and (*b*) stipple and polychromatic red cells. More complex methods are required in certain of the more highly dangerous lead hazards, *e.g.*, volatile organic lead compounds.

The expertise to do this is minimal, and a junior boy or girl can be trained to do it and even interpret the findings in a short time. If the conventional method by transmitted light be used, then it should be realized that the polychromatic cell is a stipple cell with the stipples very closely set, and they should be counted together, and can readily be confirmed by dark-ground examination (Figs. 4 and 5).

Haemoglobin determination alone is not sufficient, for many patients are found with 100 to 90% haemoglobin who may be presumed to be absorbing lead from the high (stipple and polychrome) counts. Nor

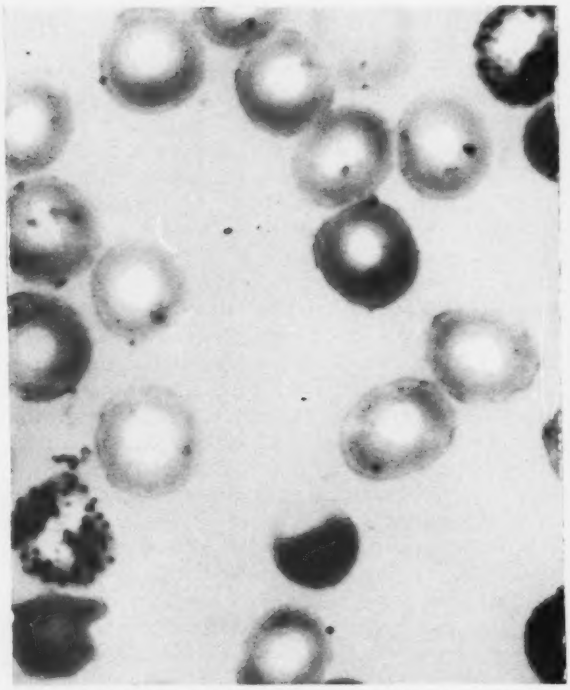


FIG. 4.—Rabbit blood stained with alkaline methylene blue and photographed by transmitted light showing various-sized basophilic (polychromatic) cells due to chronic lead exposure.

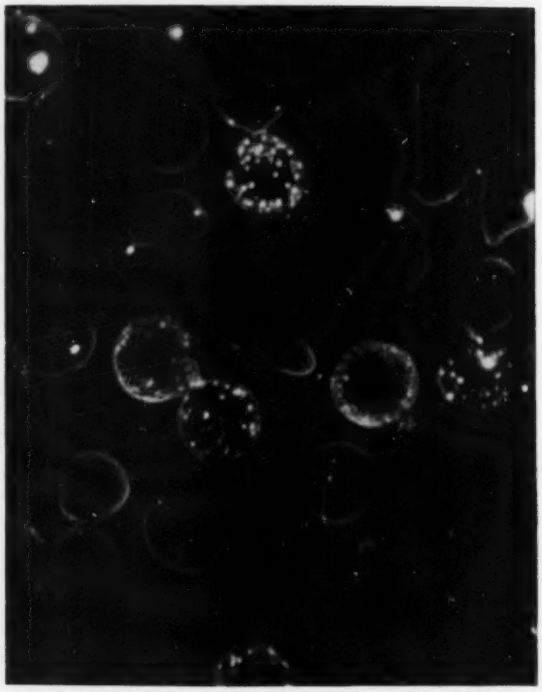


FIG. 5.—Rabbit blood stained with alkaline methylene blue and photographed by dark ground illumination showing ease of recognizing stipples (golden granules) and two polychromatic cells; the polychromatic cells are manifestly very finely stippled cells.

is the stipple and polychromatic count sufficient, for a relatively low cou t is frequently found with a very low haemoglobin (Fig. 6).

The second proposition is that it is not difficult to prevent the notification of cases of lead poisoning by removing men from exposure at a critical moment and giving them other work. This is, in fact, what happens in most factories with a hazard from lead.

Since in most cases rapid recovery is the rule, the statistics of lead intoxication can be kept low, and the national returns become valueless as far as a national industrial picture of lead absorption is concerned. Moreover, men kept on at work in spite of evidence of lead intoxication do not develop a proper respect for lead and hence develop recurrent attacks of lead poisoning (see also Fullerton, 1952) (Table 2). As a rule (this is my third proposition) no man at work makes as good or as quick a recovery from lead intoxication as he does at home or in hospital (Table 3), so the importunities of men to be kept at work in spite of evident lead intoxication should be resisted and they should not be allowed to return to work until the normal blood picture is re-established. The recent introduction of chelating agents may expedite recovery and return to work (Foreman, Hardy, Shipman, and Belknap, 1953).

Kehoe (1951) has emphasized that the usual forms of lead intoxication are self-limited, of relatively short duration, and that there is complete recovery when the exposure has been terminated, and that no irreversible damage to the blood-forming tissues is associated with plumbism. The cases to which this statement would not apply are the now exceedingly rare encephalopathies and muscle palsies.

Fig. 7 shows the kind of picture one would wish to avoid, that of a man who took five years to recover his haemoglobin although removed from contact with lead (see also Fullerton, 1952).

Fig. 8 shows the data on a case of some interest. Three months of work on lead were followed by a fairly acute episode from which the patient was allowed to recover while still at the factory doing odd jobs not involving contact with lead. In spite of a very big drop in the number of stipples and polychrome cells, the haemoglobin level recovered poorly. A subsequent period on work with lead again led to an episode which was certified. Certified as fit to work after 21 days, the patient was again

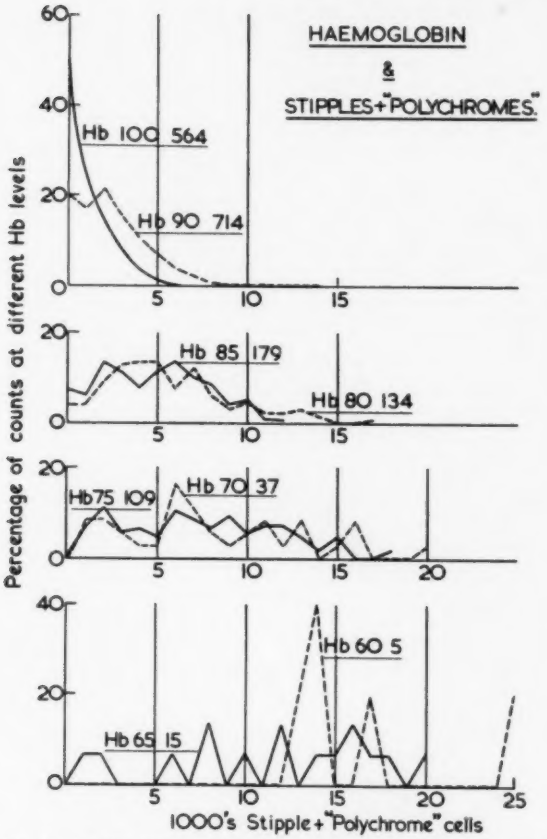


FIG. 6.—Relation between haemoglobin and stipple-polychrome counts in workers exposed to a lead dust hazard. Numbers of bloods examined shown with Hb values. (See text).

maintained in the factory on work involving no contact with lead till the haemoglobin was about 85%. A period on lead again threatened an episode, and subsequently a change to permanent work elsewhere led to a slow and unsatisfactory recovery to almost 90% haemoglobin in about two years.

Finally, it is important to remember that there are men who are remarkably reactive to even small amounts of lead. This is seen well in Fig. 9 which shows the blood findings in a worker who reacted at once when given work on a lead process, showed great falls in haemoglobin without a simultaneous rise in stipples, and who oscillated violently even when on work not involving a lead hazard. Lane (*loc. cit.*) and others have described cases of hypersensitivity and referred to evidence of family susceptibility to lead. A full study of such cases would be of considerable interest. The influence of alcohol must not be forgotten.

My fourth proposition is that the changes in the peripheral blood in lead intoxication are due to changes in the bone marrow.

The stippled red cell derives from stipple normoblasts in the marrow, both of which may be seen in the circulating blood (Figs. 10 and 11). The stipples of a normoblast in the bone marrow are seen as a corona round the nucleus for mitosis occurs in the stippled normoblast apparently normally.

There are far more stipple cells in the bone marrow per million erythrocytes than in the circulating blood during lead intoxication. Pirrie (1952), using guinea-pigs, found as many as 55% of haemoglobinating normoblasts in the marrow showing basophil stippling when only 2·5% of red blood cells were

TABLE 2

LOST TIME OF TWO GROUPS

Certified*								Uncertified†							
Year	No.	Name	Time Lost	Year	No.	Name	Time Lost	Year	No.	Name	Time Lost	Year	No.	Name	Time Lost
1936				*1940*				*1936*				*1939*			
	1	F.G.			12	W.C.	3 days	28 : 10	1	*E.E.*	Nil	23 : 1	16	*C.F.H.*	Nil
	2	W.P.	8 days		13	A.H.T.	1 mth.	9 : 12	2	*E.E.*	Nil		17	A.E.P.	20 days'
	3	G.F.K.	10 days				13 days	4 : 11	3	*W.F.*	Nil				investigation
	4	J.S.	2 mths.	*1941*	—	—	—		4	*F.G.*	Nil		18	A.W.	Nil
1937				*1942*	—	—	—	14 : 10	5	*F.K.*	Nil	*1940*			
	5	S.F.	26 days					28 : 10	6	*F.K.*	Nil	23 : 9	19	*H.J.*	Nil
	6	K.A.M.	15 days	*1943*					7	H.E.W.	8 days		20	G.M.	Nil
	7	A.W.	16 days	20 : 11	14	*G.F.M.*‡	1 mth.			(Hb. 75%)	gastritis	*1941*	—	—	—
	8	P.N.	2 mths.				4 days	*1937*							
			6 days					24 : 3	8	*W.F.*	Nil	*1942*	—	—	—
1938				*1944*				5 : 5	9	*W.F.*	Nil				
	9	T.H.	13 days	17 : 4	15	*G.F.M.*	30 days		10	*F.G.*	Nil	*1943*			
			18 days						11	C.J.H.	Nil	22 : 5	21	*H.J.*	Nil
1939									12	J.L.	Nil				
	10	E.M.	28 days						13	R.O.	Nil	*1944*	—	—	—
	11	F.H.W.	1 mth.					*1938*							
			21 days					13 : 12	14	*C.F.H.*	Nil	*1945*			
									15	W.R.	Nil	26 : 1	22	*H.J.*	

*Certified = recovery away from factory, †Uncertified = recovery at work.
(All cases 60–65% Hb at time of certification or action in factory.) ‡Recurrent cases in italic.

TABLE 3

PERIOD OF RECOVERY OF Hb

	Maintained at Work	Removed to Home or Hospital
No. of Cases ..	24	9
Hb at time of transfer	65–70%	65–70%
Mean time to reach 80% or more	1·93 months (3 weeks–7½ months)	1·66 months (16 days–2½ months)

Indicates slight advantage of getting man away from factory even on light and non-lead work.

1 case of Hb 43–45% recovered to 80% in 28 days whilst at work on non-lead.

stippled in the stained peripheral blood. Similar findings were obtained in our experiments with rabbits. Even in heavy exposure to lead not all the normoblasts show stipples, many proceeding to normal haemoglobination. Stipple cells, polychromatic cells, and reticulocytes all owe the appearances seen to ribonucleic acid. This can be shown by treating the cells with ribonuclease which completely removes the basophilic material and leaves the cells uniformly acidophil. In the normal maturation of the erythrocyte, the basophilic substance in the cytoplasm practically disappears at the reticulocyte stage, and haemoglobination is completed without a hitch.

The delivery of "leaded" basophilic cells from the marrow into the circulation is gradual in ordinary circumstances as the peripheral cells are removed. This statement applies to reticulocytes, polychromatic cells, and stipple cells, and it must be clearly understood that the particular appearance associated with these cells is not preformed, but depends upon the method of staining and upon the amount and state of the basophilic substance. Conditions suitable for staining one kind of these cells may fail entirely for the others.

If blood rich in reticulocytes is stained supravitally with brilliant cresyl blue the usual picture is obtained of a filamentous-granular network but if a dried film is stained with the same dye the reticulocytes are seen as cells with vacuolated basophilic material (Figs. 12 and 13). Stained supravitally or in dried film stipples are readily seen in their usual form in red blood cells as well as in normoblasts. Reticulocytes stained in dried film and examined in the dark ground show a finely granular or finely reticular pattern with irregular vacuoles.

MacFadzean and Davis (1949), Pirrie (*loc. cit.*), Rimington (1938), Kench, Lane, and Varley (1952), Dustin (1942), and others have gone far to elucidate the nature of the stippling property of the erythrocyte in lead absorption.

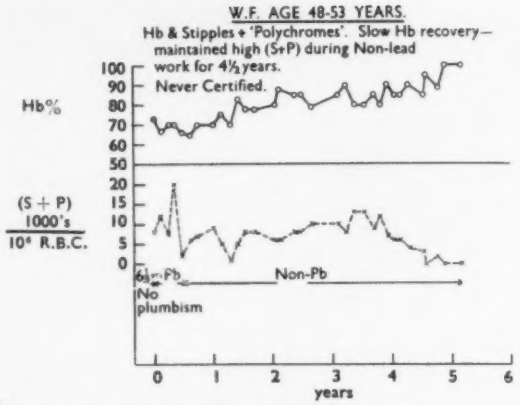

W.F. AGE 48-53 YEARS.
Hb & Stipples + 'Polychromes'. Slow Hb recovery—maintained high (S+P) during Non-lead work for 4½ years.
Never Certified.
Hb%
(S + P) 1000's / 10⁶ R.B.C.
Non-Pb
No plumbism
years

FIG. 7.—Case of lead anaemia showing extremely slow recovery of haemoglobin whilst maintained at work.

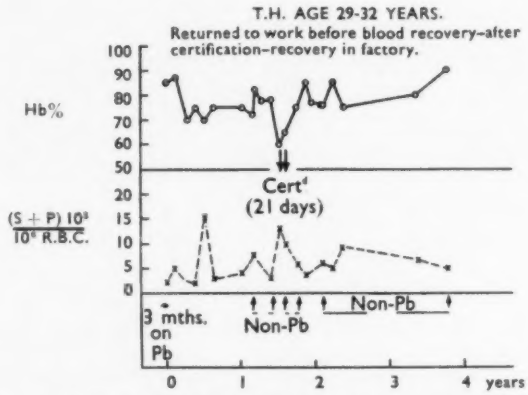


FIG. 8.—Case of certified plumbism considered clinically fit to return to work, but thereafter requiring almost two years to regain a stable Hb on non-lead work.

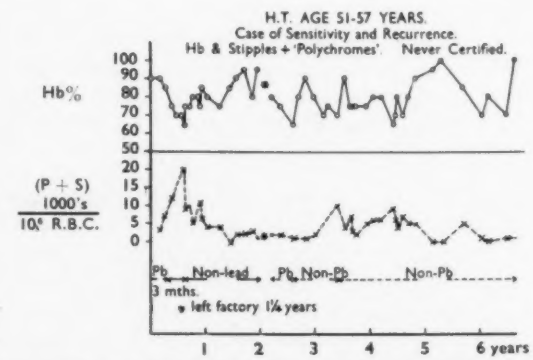


FIG. 9.—Case of sensitivity and recurrent lead anaemia in spite of long periods on non-lead work. Close correspondence of Hb and stipple values.

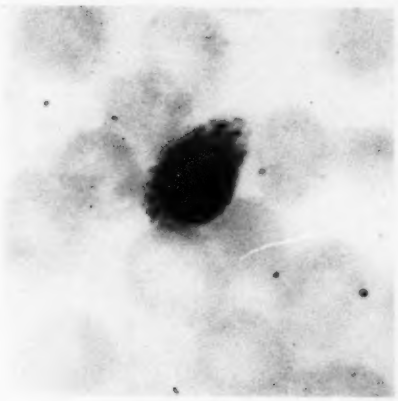


FIG. 10.—Rabbit blood after chronic lead inhalation showing stippled normoblast. Stained with alkaline methylene blue. × 2000.

FIG. 11.—Rabbit bone marrow after chronic lead inhalation showing coarsely stippled normoblast (R.B.C. somewhat out of focus). × 2000.

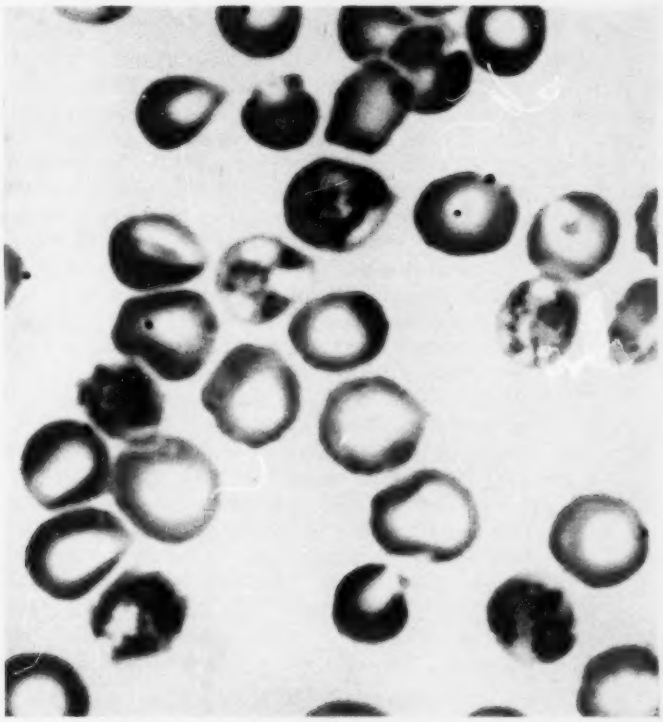


FIG. 12.—Rabbit blood after chronic lead inhalation showing reticulocytes; supravital staining with brilliant cresyl blue. × 1200.

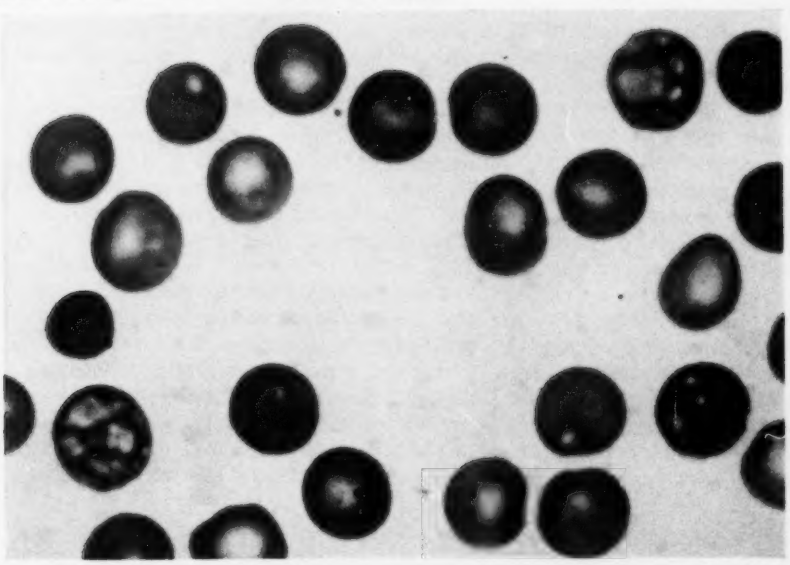


FIG. 13.—Rabbit blood on same occasion as Fig. 12 (dry film stained with brilliant cresyl blue) in which reticulocytes are seen as cells with vacuolated basophilic material. × 1200.

Lead poisons the later precursors of the red cell and intoxication manifests itself as (1) retention of basophilic material instead of its almost complete disappearance at the normoblast and reticulocyte stage and completion of maturation. (2) The so-called stipple cell and the polychromatic cell derive from the failure of maturation of the basophil normoblast. The reticulocyte derives from non-poisoned normoblasts. Since reticulocytes may increase before lead anaemia and stippling are established we may assume that the stipple and polychrome cells indicate a failure of the normoblast to go on to the reticulocyte stage. With the failure of the bone marrow in extreme cases of lead poisoning, stipples, polychromes, and reticulocytes all fail. This is why stipple counts fall in the last stages of very severe lead poisoning. (3) By processes not properly understood (synthesis of porphyrin, incorporation of Fe into coporphyrin III to form haemoglobin, etc.) lead inhibits the full haemoglobination of red cells. (4) Evidence of abnormality of red cells in lead absorption is that they show (*a*) diminished fragility in being able to withstand lower salt concentrations ; (*b*) increased brittleness and less durability in the conditions of existence in the circulation. In addition, they are readily taken up and destroyed by the spleen and other reticulo-endothelial cell locations. (5) Lead anaemia is due to (*a*) poor haemoglobination and (*b*) greater destructibility of cells containing lead.

Industrial Enzyme Poisons

Many industrial poisons are enzyme inhibitors, *e.g.*, cyanide, organic arsenicals, organo-phosphorus compounds. The clinical pictures of acute poisoning can sometimes be related more or less specifically to the inhibition of particular enzyme systems.

The most important of these has, in recent years, been the large group of organic phosphorus insecticides (Fig. 14) and potential war gases. Since there is intense competition in this field of manufacture, chemical research is directed towards synthesizing compounds which combine a broad spectrum of high insecticidal activity with low mammalian toxicity.

The toxicity of these compounds (Table 4) is attributable to their inhibition of cholinesterase and hence the clinical picture of poisoning is that of poisoning by endogenously produced acetylcholine. But the degree to which they inhibit the enzyme *in vitro* is in some cases many (even millions of) times less than would be expected from their toxicity *in vivo*. Transformation into highly potent anti-cholinesterases occurs in these cases in the liver.

Recently progress has been made towards evolving organo-phosphorus compounds possessing low mammalian toxicity compared with the now classical

TABLE 4

L.D.50. ORGANO-PHOSPHATE INSECTICIDES*

Compound	Oral L.D.50	I.P. L.D.50
T.E.P.P.	1·2 R.f. 2·0 R.m.	0·65 R
Paraoxon	3·5 R.m.f.	1·2 R.m.f.
Dimefox	5 R.m.	
Systox (Commercial) ..	6·39–9·7 R.m.	4·5–8·37 R.m.
>P(=S)–O–	7·5 R.m.	
>P(=O)–S–	1·5 R.m.	
Pestox (O.M.P.A. Schradan)	9·7–10·0 R.m.f.	8·0–8·5 R.m.f.
Parathion	6 R.f. 15 R.m.	4 R.f. 7 R.m.
E.P.N.	14·5 R.f. 91·0 R.m.	50 M.
Mipafox	$< {}^{1}/_{20}$ Parathion	
Malathion	2,420 R.f. 2,860 R.m.	750 R.

*Median lethal doses of organo-phosphate insecticides.
R = rats, M = mice, m = male, f = female. All values in mg./Kg.

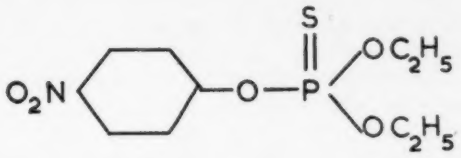
parathion and tetraethyl pyrophosphate (T.E.P.P.). Thus " mipafox ", which is the mono-isopropyl analogue of " dimefox ", is perhaps 25 times less toxic than " parathion ", and " malathion " about 200 times less toxic to mammals. The optimism engendered by these facts is tempered in the case of " malathion " by its less potent insecticidal properties and in that of " mipafox " by pathological considerations.

The questions which must be answered by the industrial investigator in respect of these and other agents which are applied to food or crops are : (1) Do they constitute a risk to the consumer of the food products ? This has been adequately answered in the report of the working party appointed by the Ministry of Agriculture (1953) which gives the necessary assurance but recommends investigation of the maximum permissible residues arising from the use of toxic substances. (2) Do they constitute an unjustifiable risk to the user ? The answer here is no, provided that the necessary precautions are implemented, and, in addition, if the use of atropine is properly understood by employer, supervisor, and doctor as the specific therapeutic agent for the parasympathetic signs and symptoms (Goldblatt, 1950, 1951).

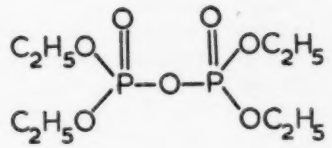
The onset of symptoms depends upon the level of true cholinesterase in the blood cells, brain, and nervous tissues, in nerve fibres and at motor end-plates and, of course, at ganglionic synapses. Since a great fall in the enzyme may occur in some individuals without any manifest signs or symptoms, it is essential that the blood cell cholinesterase of exposed persons should be determined as a routine

ORGANO – PHOSPHORUS INSECTICIDES

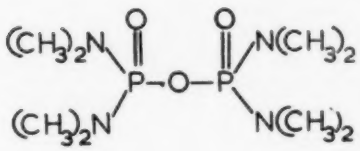
1). PARATHION



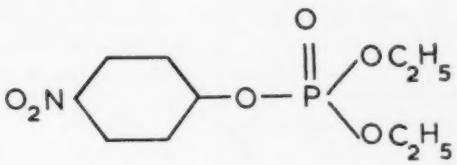
2). T.E.P.P.



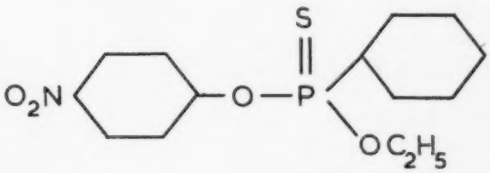
3). PESTOX



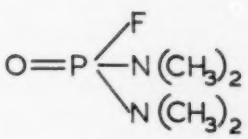
4). PARAOXON



5). E.P.N. (U.S.A.)

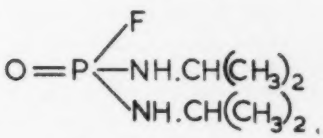


6). DIMEFOX



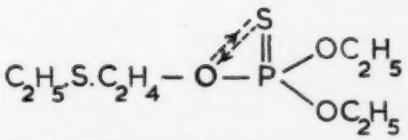
SYSTEMIC

7). MIPAFOX



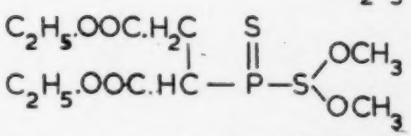
SYSTEMIC

8). SYSTOX



SYSTEMIC

9) MALATHION



LEAST TOXIC

FIG. 14.—Formulae of active compounds in organo-phosphorus insecticides.

in order to preclude a fall to dangerous levels ; each subject should be his or her own control. The variance from mean levels in populations is too great to draw conclusions from single observations. It is so easy to ignore the early symptoms which may be no more than a slight tightness in the chest and a sense of mild apprehension. This is the more important since in irreversible inhibition of cholinesterase there is considerable delay before the normal enzyme level is regenerated. In the case of " mipafox " poisoning it may take 50 to 90 days to recover the initial red blood cell level of cholinesterase after an acute severe attack.

Until very recently it would have been held that the organo-phosphorus insecticides did not produce chronic effects, acute non-lethal attacks passing off without sequelae and long-term administration of sub-lethal doses to animals giving rise to no chronic toxic phenomena. Clinical observation and experiments had shown that among organo-phosphorus compounds D.F.P. (di-isopropyl-phosphorofluoridate) and T.O.C.P. (tri-*o*-cresyl phosphate) both in man and in animals could induce demyelination in the cord and in the brain, and although suspicion was cast, by analogy, on the phosphorous insecticides, it was not till 1951 that a case of paralysis due to " parathion " was described in Germany by Petry (1951) and two cases due to " mipafox " [bis-(mono-isopropyl) phosphorodiamidic fluoride] in this country by Bidstrup, Bonnell, and Beckett (1953), none of which appears to have recovered in some three years.

The addition of these agents to the already known diversity of demyelinating agents in man and animals (carbon monoxide, arsenicals, sulphanilamide, spinal anaesthetics, vaccination) tends to turn us from a purely chemical hypothesis to perhaps an enzymatic one. Demyelination has been produced experimentally with CO, KCN, N_3Na, N_2O, and repeated doses of barbiturates (Weston Hurst, 1941, 1944).

The paralysis which followed " parathion " and " mipafox " resembled that described among many people who had absorbed T.O.C.P. in one way or another, and in both these groups it seems probable that the persistent signs were due to demyelination.

Fig. 15 shows a section of the cord of a fowl (1·35 kg.) treated with a single dose of 0·5 g./kg. of tri-*o*-cresyl phosphate (T.O.C.P.). This and another fowl similarly treated were observed for over 250 days. The phenomena were of the same kind as found with the anti-cholinesterase insecticides. Some recovery was observed, especially in respect of secondary sex characters and egg-laying power, and to some extent in muscular powers, but this was very slow and only partial (see also Barnes and Denz, 1953).

The selection of a special tract for attack is puzzling and not less so than in man, in whom the whole picture is of a motor disturbance. In the cases due to insecticide a neuromuscular block due to the breakdown of the normal relation of cholinesterases and their substrates was first seen and later a peripheral neuritis with only those sensory impairments as are normally associated with polyneuritis.

As more and more compounds are being synthesized, it is important not to assume the relative safety of a given compound until acute and chronic

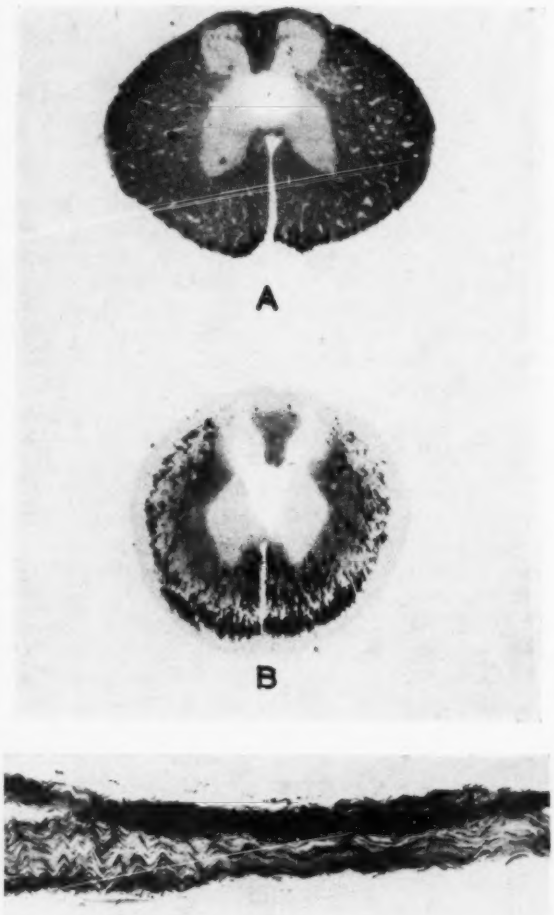


FIG. 15.—Cervical cord and sciatic nerve of a fowl treated with a preparation of tricresyl phosphate calculated to contain 0·1% of the ortho-isomer. Total dose in 16 days = 2 mg./kg. by mouth. First paralytic signs in 21 days followed by progressive worsening of paralysis of legs. Demyelination in anterior and lateral columns and markedly on sciatic cord. × 12. Marchi's method. A = upper, and B = lower, cervical cord below sciatic nerve.

experiments have been carried out, and also the effect on the nervous system studied in detail in a variety of animal species.

Occupational Carcinogenesis

There are very few identifiable agencies which have been shown without any doubt to be carcinogens to man. These are arsenical compounds, radiations (*x*-ray, radium, ultra-violet light), β-naphthylamine, benzidine, and probably 3·4 benzpyrene.

Of the host of compounds and complex mixtures which have produced tumours of skin, liver, mammary gland, lung, and bladder in animals, only these have been demonstrated as direct or indirect human carcinogens. The active agents in such carcinogenic products as tar, lubricating oil, soot, pitch, are not established with certainty, although the isolation of 3·4 benzpyrene from tar casts strong suspicion on this compound.

Long-continued therapy with arsenical preparations and work with arsenical compounds have led to indubitable skin changes (hyperkeratosis) and finally to epitheliomata. But no convincing experiment has been published to demonstrate a similar effect in animals.

In the case of certain radiations, neoplastic change as well as severe blood changes have undoubtedly followed long exposure in man and in animals, though the tumours which develop are different—sarcomata in animals and carcinomata in man. The differences are attributable to the different tissues reached by the radiation.

Neoplastic changes, sometimes benign but most often highly malignant and recurrent, in the bladders of workers exposed for varying periods to the fume and/or dust of certain aromatic amines have been reported for nearly 60 years in all parts of the world where organic dyestuffs are manufactured. This clinical fact has been confirmed by experiment both in the U.S.A. and in Britain with dogs in which identical bladder tumours were induced by feeding β-naphthylamine. It has been suggested by Bonser, Clayson, and Jull (1951) that the incidence of bladder tumours inducible by treatment with β-naphthylamine in different species is roughly related to the amount of urinary conjugates of 2-amino-1-naphthol excreted.

More recently the same suspicion fell upon benzidine and has been amply confirmed. Intensive research both inside and outside industry has led to the demonstration of the carcinogenic properties of benzidine in rats (rectum, sebaceous ear glands, liver) but bladder tumours had until recently not been induced except in the case of one dog (Spitz, Maguigan, and Dobriner, 1950). The possibility that here also the *o*-hydroxyamine is the immediate carcinogen has received much consideration.

The contribution made to the elucidation of the problem in this country has been notable and the names of Bridge (1934), Macalpine (1929,) Wignall (1929), Walpole, Williams, and Roberts (1954), Scott (1952), Baker (1953), Bonser and others, (1951), Bonser, Clayson, Jull, and Pyrah (1952) and more recently Case and Hosker (1954), and Case, Hosker, McDonald, and Pearson (1954), will always be remembered for the great light shed upon it. The total number of cases which Case and his colleagues (1954) were able to trace in the chemical industry between 1900 and 1952 was 455. Case's classical statistical investigations are a model for the future investigation of occupational diseases. Case and others have established on a national scale what others have found in industrial practice both in this country and elsewhere. Contact with the naphthylamines or benzidine is now fully recognized as a carcinogenic hazard, and aniline appears to be exonerated. Some as yet cryptic factors in the manufacture of magenta and auramine appear to throw suspicion on both these processes. The disease was prescribed as an industrial disease in 1953 in this country, just 58 years after the original description by Rehn. It is proper to record the unremitting clinical control by Dr. Charles Cresdee for almost a quarter of a century in one very large centre where these compounds were manufactured, which has been a guide and an inspiration to those who have had to pursue the problem in the quiet of the laboratory (for earlier work and review see Goldblatt, 1947, 1949).

More recently, arguing very ingeniously from the fact that these tumours had formerly been attributed to aniline, which until now has not been proven to be a bladder carcinogen, Walpole, Williams, and Roberts (1954) in Manchester came to suspect 4-amino diphenyl, which had been found in residues in aniline manufacture 80 years ago, as the probable cause. Experiments on dogs confirmed the presumed bladder carcinogenicity of this compound.

Certain condensation compounds of the naphthylamines formerly used in the processing of rubber have already been banned by manufacturers since new knowledge on the previously suspected but uninvestigated incidence of vesical tumours in the rubber industry became available (Case and Hosker, 1954).

Both the Leeds and Manchester workers have come to place great emphasis on *o*-hydroxyamines as the effective bladder carcinogens. This has opened a large speculative field of inquiry, because

a considerable number of hitherto unsuspected aromatic amines and derivatives of them could yield various *o*-hydroxyamines metabolically.

The dilemma before industry in this field is how to deal with the considerable numbers of compounds that might carry suspicion. The project of examining all the derivatives of cyclic hydrocarbons and their homologues which, in their metabolism, might yield amines or derivatives of amines of potential carcinogenicity must, however, be undertaken. There is no escape from the argument that if a compound is carcinogenic in animals, in whatever location in the body, it must be so regarded, at least potentially, in man. In some cases it is possible to circumvent carcinogenicity chemically. In the case of β-naphthylamine this has been done in this country and in some continental countries by avoiding liberation of the base at any stage of manufacture or use. Certain food azo-dyestuffs have already been rejected because of the possible metabolic fission of the relatively simple molecules with the liberation of a carcinogenic amine, in the absence of any but presumptive evidence. A systematic study of food colours on these lines is in progress in my laboratories.

In the industrial field the manner of attack must be cooperation between statisticians, industrial doctors, and experimentalists. The statistical weapon is one which is potent in the hands of specially gifted people, provided all the data are collected on a pre-determined plan and all in possession of relevant records cooperate fully. Before it is prudent to publish the view that a given material is not carcinogenic in any circumstances, it is well to remember that experienced investigators have made such statements and subsequently have been proved mistaken.

Experiment (in our hands as well as in others') has failed to show carcinogenic properties in chromates, but in the U.S.A. there is considerable statistical support that chromate dust can induce lung cancer (Machle and Gregorius, 1948) but Bidstrup (1951) was not able to draw clear conclusions from her *x*-ray survey of 724 workers in the industry in this country. Recent statistical data in the U.S.A. show that chromate workers had a mortality rate for respiratory cancer 29 times as great as would be expected among a comparable group of all males in the country (Federal Security Agency, 1953).

In 1949 the Senior Medical Inspector of Factories gave reasons for the belief that the pulmonary fibrosis in asbestosis is followed by an inordinately high percentage of cases of pulmonary cancer. It will be difficult, if the observation is confirmed, to envisage the process here as other than one initiated by local mechanical irritation but a chemical carcinogen is not ruled out although it is more difficult to find support for it. It is not sufficient to state that a given material is non-toxic. Toxicity as ordinarily understood is in some sense the reverse of carcinogenicity. For whereas a compound exercising a toxic effect on a cell is driving that cell in the direction of inanition and death, one exerting a carcinogenic effect on a normal cell is driving that cell towards excessive, if abnormal, function and, for a time, more vigorous life. This is not to say that a carcinogenic compound is never toxic in the ordinary sense, but rather that a toxic agent in full spate is unlikely to permit the establishment of carcinogenicity. Although the mean induction times for certain occupational carcinogens are long and not dependent on the severity of exposure, it is to be noted that in some individuals the induction time may be quite short and in others much longer than the mean.

Recent Work in the Diagnosis of Vesical Tumours

The need for continued medical supervision of men who have been exposed in the past to bladder carcinogens is manifest even after exposure has ceased, and even after leaving the industry.

In a section of the chemical industry exfoliative cytology is being used to detect early bladder tumours. In the U.S.A. the teaching of Papanicolaou (1947, 1948) on the importance of the recognition of neoplastic changes in exfoliated cells has been much regarded. Cells may be exfoliated from the lung, stomach, bladder, cervix, and vagina, and, provided the morphological and staining characters of tumour cells can be recognized, there is no theoretical reason why a neoplastic process should not be detectable at an early stage (see also Bamforth, 1953).

In the case of bladder tumours the early development is not attended by any disturbance of the patient in either occupational or non-occupational cases. Hence arises the need to establish routine urine examinations for microscopic blood, which is often the earliest sign of bladder irritation, of ruptured small varicosities, of a broken frond of a small papilloma, or of the slow and insidious oozing of an infiltrating carcinoma. In a small proportion of cases microscopic haematuria is unaccompanied by a tumour visible in the cystoscope, and in a larger proportion there may be no blood in spite of the presence of a tumour.

In this country it is useless to recommend routine

cystoscopy of workers as it is practised on the Continent and to some extent in the U.S.A. Hence urinary examinations must be made and every device used which will, with the minimum discomfort, give a correct picture of the inside of the organ. To this end we are seeking to enlarge the scope of urinary examinations by determining the picture of vesical exfoliation in normal subjects, by applying Papanicolaou's methods to the urine, and, we hope later, by cytochemical tests for malignancy. By methods different from those hitherto used, Mr. Rofe in my laboratories has been able accurately to stain, characterize, separate, and count the types of cells found in normal human urine (Rofe, 1955) after removal of the normally interfering organic and inorganic matter and debris and concentrating the cells in 1 in 1,500 of the volume in which they were voided. Certain conclusions may thus be stated : (1) Most normal urines contain blood. (2) Most normal urines contain leucocytes. (3) The cellular content other than these is divisible into two main parts (*a*) squamous and transitional, 15μ and over in size (urethra, bladder) ; (*b*) small epithelial cells derived from kidney and prostate (in the male) 15μ and under in size. These cells are in various stages of degeneration.

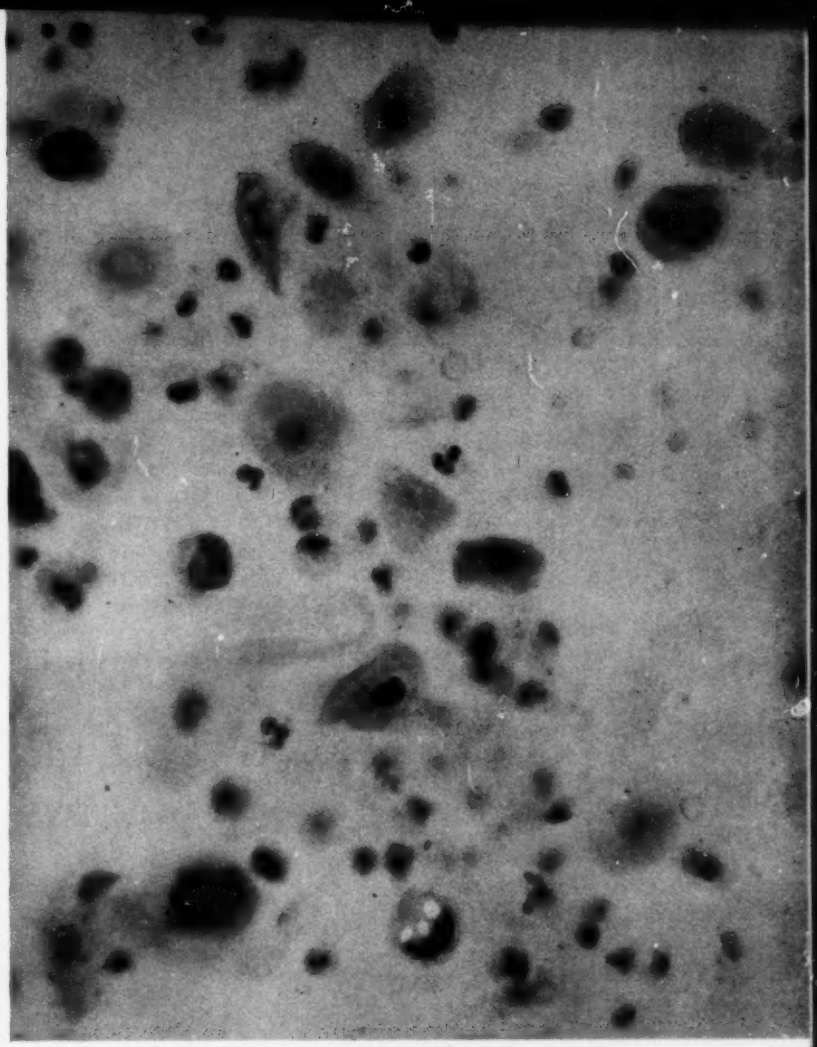


FIG. 16

A very interesting feature of these counts was that there were always far more leucocytes in normal urine than could be accounted for by a simple transudation of whole blood. This perhaps means that the bladder is always in a state of some irritation, either chemical or mechanical, which does not reach consciousness. By applying Rofe's method it is possible to see at a glance all the cells exfoliated in a given sample of urine. Having a reliable picture of the normal cell content, deviations from it can the more readily be recognized and the detection of exfoliated tumour cells is facilitated by the small volume into which the cells are concentrated. The character of exfoliated bladder tumour cells has been described by Crabbe

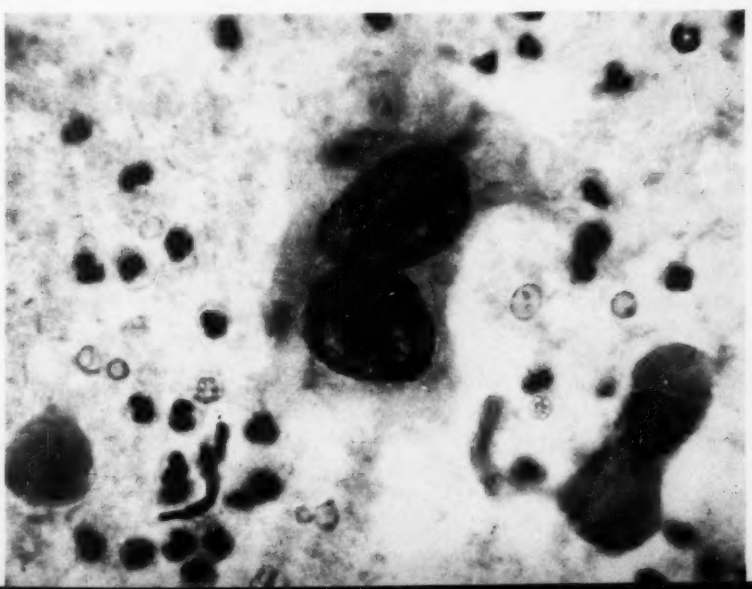


FIG. 16.—Smear from urine of worker in manufacture of dyestuff intermediates showing erythrocytes, polymorphs, abnormal and degenerated epithelial cells, and several definitely malignant cells. Papanicolaou's technique of preparation and staining. × 500.

FIG. 17.—Smear from another dyestuff worker showing erythrocytes, many polymorphs, and giant binucleated malignant cells. Papanicolaou technique. × 500.

FIG. 17

(1952) working in my laboratories. The value of cytological diagnosis has been amply demonstrated.

The cytological criteria laid down by Papanicolaou for the diagnosis of malignancy include increased size and bizarre shapes; enlargement of nuclei in relation to cytoplasm; altered nuclear and chromatin pattern; increased affinity of nuclei for basic stains; and variation in nuclear sizes in a group of cells (Figs. 16, 17). In a method of diagnosis of this kind the danger is the false negative. The false positive is less serious, but always of great interest, especially when found in the absence of blood cells and cystoscopically visible tumours. The cystoscope is not infallible, for we have had cases in which a positive cytological diagnosis was subsequently confirmed by cystoscopy after initially negative cystoscopic reports.

It is becoming clear that the exfoliation of cells from new growths is not a uniformly constant process. One day it may be prolific, another relatively unproductive. Further, the ease of recognition of neoplastic character varies.

For these and other reasons we prefer at this stage to base judgment on a combination of the classical search for haematuria and to fortify it with the cytological method. It has thus been possible to assert the presence of a tumour at a stage when a slight microscopic haematuria would have left us in doubt and the patient in delay.

Field Experiment

Field investigation is properly the domain of the industrial doctor, and it is the most difficult.

In the last analysis it is upon field investigation that a final judgment must rest as to the relation between industrial environment and state of health. The difficulty does not lie in the recognition of this proposition, but in obtaining the opportunity and in devising the appropriate methods to establish such relations. To attain results which are soundly based and generally acceptable is a task requiring the cooperation of many disciplines. In the main, therefore, it is in the big organization with great resources that such studies can be made, but it is a parallel fact that in such organizations the environmental conditions are likely to be the best.

The practical application of the principles which emerge from field studies requires assiduity on the part of the industrial doctor and of those responsible for industrial hygiene, for this requires not only the willingness of employers to make money available, but also the willingness of workers to create it.

In conclusion, my object has been to indicate some of the things which concern those who are engaged in research in industrial health in the chemical industry, and some of the difficulties and dilemmas which arise. This kind of work is merely the preliminary to the application of the knowledge thereby obtained in the field and the factory. It is there that the ultimate goal set by James Mackenzie must be reached—the prevention of occupational illness.

I am extremely indebted to Mr. Kenneth Cooper and Mr. Leslie Hewitt for their kind cooperation in the preparation of the photomicrographs, and to my colleague Dr. J. G. S. Crabbe for Figs. 16 and 17. My thanks are due to Mr. Berczy, Mr. Crozier, and Mr. Denks for much technical assistance.

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MANGANESE POISONING IN MOROCCAN MINERS

BY

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While there is very little in the literature about criminal or accidental manganese poisoning, manganese ores and their industrial applications give rise to a number of cases of occupational poisoning. The historical background of the condition has already been reviewed in a previous paper (Rodier and Rodier, 1949) but it should be noted that this occupational disease has been recognized since 1837 when Couper of Glasgow observed the first cases among five manganese ore crushers. He described a series of nervous phenomena : muscular weakness, paraplegia, tremor of the extremities, a tendency to lean forward while walking, whispering speech, and salivation.

Since then a number of writers have made further observations and recognized manganese as a poison affecting the central nervous system. It is less well known than other metallic poisons. It continues to be rare since only a limited number of workers come in contact with manganese in a dangerous form. The symptoms, which progress as a rule to total disablement, render it one of the most serious occupational hazards. It poses important social problems, as much concerning the rehabilitation of partially incapacitated labourers, as the care of the sick man and his family by the community.

Manganese and its Ores

Manganese is not found in a free state in nature but its minerals are quite numerous. Manganese dioxide has been known since remote antiquity and Pliny mentions its use in glass making. In 1774, in Stockholm, Scheele defined the nature of the metal after three long years of research. After Bergman's thesis (1774) the chemical existence of manganese was finally established. It was in 1785 that Guyton de Morveau proposed the name " manganese " to distinguish the metal called " magnesium " by Bergman. The metal is extremely diffused in nature under mineral and organic forms. Some writers consider it invariably present in arable soil, and it seems to be an almost constant constituent of living matter.

Although manganese in its pure form is of limited use, its derivatives are much in demand in industry. The alloys which it forms with certain metals, and to which it confers remarkable properties, give it great industrial importance. The metal industry could not dispense with it, and uses an average of 14 kilograms of manganese per ton of ordinary steel. Alloys of iron and manganese (ferro-manganese and speigel) play a very important role in steel works as desulphurants and de-oxidisers. Ferro-manganeses also serve in the preparation of numerous special steels with copper, aluminium, and other metals.

Outside metallurgy certain special categories of derivatives called " chemical manganese ", including those varieties richest in bioxide, are used as depolarizers in the manufacture of dry cells. The pyrolusite is used in small quantities in the glass industry as a decolorizer under the name of " glass maker's soap ". Its oxidizing action on the unsaturated fatty acids is used in manufacturing quick-drying paints. The chemical industry also uses the pyrolusite as a catalyst and an oxidizer. Finally, in electro-technology manganese is used for making certain types of electrodes for electric soldering. If at the present time the U.S.S.R. share is estimated to be perhaps 3,000,000 tons, world production is of the order of 7,000,000 tons of saleable ore. Of this total the British Commonwealth easily leads with 2,400,000 tons, thanks to India, the Union of South Africa, and the Gold Coast. Other producers are Morocco (5%), Brazil (3·5%), Egypt (2·5%), and Cuba (2%). The U.S.A., a big consumer, produces very little, less than 100,000 tons a year.

Production of Manganese in Morocco

Production in Morocco is developed under the influence of the French Protectorate. From 760

tons in 1922 it reached by 1953 420,000 tons, of which 40,000 tons are chemical salts.

The mines of Imini, Bou-Arfa, and Tiouine (in order of importance) furnish 90% of Moroccan production. Geologically the deposits of manganese in Morocco are of two principal types, sedimentary deposits and seam deposits.

The first are the more important and make up the greater part of the country's production. They are situated in cretaceous terrains such as Imini and Talsdremt, liassic as at Bou-Arfa, or cambrian as at Tiouine (Rodier, 1950). Reserves of these deposits would amount to 15,000,000 tons.

Exploitation

The techniques vary in different mines. Most of the workings at Imini are underground. The friable and powdery nature of the ore only very rarely calls for blasting or the use of rock-drilling machines. Formerly excavation was by hand-pick but now hand-picks have been replaced by pneumatic drills. The ore is removed in tubs winch-hoisted up an incline. One part only is worked as open-cast. The mineral extracted is made up of pyrolusite very rich in manganese. Formerly the ore was screened and hand-picked but now this process is replaced by pneumatic washing. The inconvenience of this system is to get rid of the quantities of dust so it has been necessary to add to this an elaborate apparatus, which seems satisfactory, for suppressing the dust.

The powdery nature of the ore renders its transport difficult and is a serious handicap to its use in blast furnaces. It is thus necessary to treat it in Casablanca in a " sinterization " works using a Dwight-Lloyd machine.

At Bou-Arfa working is by horizontal terraced trenches. The general character of the ore is rather friable and as much as a third of production is made up of small stuff.

At Tiouine workings are entirely underground and mined by the gallery-and-pillar method. Because of the hardness of the rock, excavation is by blasting after the blast holes have been bored by rock drills. The spoil is removed by mine tubs on the level, which are subsequently pulled to the surface by electric winches. Sorting of the large blocks of ore is done by hand-picking.

Personnel

The employees of the mines vary according to the size of the different centres. Table 1 gives their distribution according to their categories and the mines :

TABLE 1
DISTRIBUTION OF MINE WORKERS

	Imini		Bou-Arfa		Tiouine	
	Basic	Day	Basic	Day	Basic	Day
Men	895	421	804	362	398	189
Youths under 20 ..	90	80	19	9	52	24
Women	—	179	—	46	—	99
Office workers and supervisory staff ..	20	57	—	69	—	36
Total	1,742		1,309		798	

About 4,000 workers are thus employed in the industry. While the numbers of Europeans are relatively fixed, the numbers of local day-labourers fluctuate a good deal. Absenteeism is considerable, especially at festivals and harvest times. Numbers employed in other workings, especially the seam deposits, amount to some 500 but statistics of these are difficult to establish because the workings are constantly changing as the seams peter out.

Aetiology

The 150 cases of poisoning which I have seen have all been in underground workers. Of the various jobs at the face, undoubtedly drilling blast holes is most dangerous. This work, which used to be done by sledge hammer and hand bar, is now only carried out by pneumatic drills. Among my patients 132 were miners using these drills. The 19 others were underground labourers who mostly worked in the immediate proximity of the drills. A few of them were specialists in tamping and firing the explosives. They were thus called upon to stay in an atmosphere full of the dust resulting from blasting.

It is thus clear that the incidence of the poisoning is intimately linked with operations for pulverizing the ore and that this begins with boring blast holes and blasting itself. This agrees with the observations of other writers on the subject who have referred to the condition as " manganese crushers' disease ".

The Neurological Syndrome

The Onset of the Disease.—Table 2 shows the delay among patients before the onset of symptoms. These details were obtained in 115 of the patients.

Table 2 also shows that the onset may be quite soon after one or more months of work. Usually it comes on after one to two years of exposure to manganese and only rarely after so long as a decade. In general its onset is slow and progressive, but occasionally it will appear suddenly within a week accompanied by severe lumbar pain.

TABLE 2

DELAY BEFORE ONSET OF DISEASE

Time Employed	No. of Cases
1 to 3 months	6 (5·2%)
3 to 6 months	16 (13·85%)
6 to 12 months	15 (13·05%)
1 to 2 years	28 (24·35%)
2 to 3 years	14 (12·15%)
3 to 5 years	14 (12·2%)
5 to 10 years	20 (17·46%)
Over 10 years	2 (1.70%)

TABLE 3

SUBJECTIVE SYMPTOMS

Sexual symptoms	83%
Asthenia	77%
Somnolence	57%
Anorexia	56%
Muscular pains	51%
Headaches	38%
Mental excitability	16·5%
Fatigue	11%

The disease can be described in three phases: the prodromal period; an intermediate phase corresponding to the onset of the earliest objective symptoms; and the period of complete establishment characterized by severe disorders leading to permanent disablement.

Prodromal Period.—The first disorders are subjective. The worker complains of general asthenia and anorexia. Associated movements become more difficult to carry out and require sustained effort. This leads him to economize in such movements. He grows apathetic and dull, losing any desire to talk to his workmates. This manifestation is particularly characteristic in otherwise very talkative subjects.

Quite often there is a period of mental excitement, which may lead the man's relatives to suppose him deranged, and this may be called the "manganese psychosis". The gait is at this time staggering, talk incoherent and logorrhoeic, and the patient becomes aggressive. At the same time a period of sexual stimulation may be manifested followed usually and quickly by impotence. This last feature is met with in nearly 80% of patients, and quite often among miners in contact with manganese. A period of apathy supplants these phases of excitement. The patient is not concerned about his condition, and this indifference becomes more marked as the disease progresses.

A marked somnolence is also observed, most often to be replaced later by stubborn insomnia. Lumbar pain and cramps in the lower limbs are frequent. These pains are made worse by effort. Some patients complain of headaches and giddiness.

Despite the difficulty in taking histories, due mainly to the patients' slowness of speech as well as their great emotionalism, the symptoms have been classified according to their incidence (Table 3).

These signs vary a great deal from patient to patient. They may be more or less clear cut, single or multiple, and appear in any order. But in general they mark the onset of the illness. In addition they reappear during the established phase, more or less accentuated. In view of the incurability of manganese poisoning their importance in the early detection of toxicity is plain. As the evolution of the disease is usually slow, their recognition makes it possible to withdraw the workman from danger before the appearance of irreversible lesions. Unfortunately, the detection of these symptoms, mostly subjective, as well as the interpretation of the results of examination, is always very difficult.

The Intermediate Phase.—In the course of the preceding subjective manifestations, or very slightly succeeding them in time, certain objective symptoms may develop. The earliest are disturbances of speech. The voice becomes monotonous, lacking pitch and modulation. Words are slow, irregular, and badly articulated. Very often there is stuttering, especially when the patient is questioned. One also finds sudden halts during which no sound emerges. After having been, as it were, "blocked" for a few moments, words can then flow again correctly. Movements of the lips and tongue are very limited. From simple difficulty in articulating words, and then stuttering, complete muteness is reached during the established phase.

Nearly at the same time as these speech disorders changes in the facies may come. These constitute the "masque manganique", a facial expression at once jovial and fixed, which gives the patient a dazed appearance.

Expression of emotion tends to disappear though it is possible to make voluntary facial movements normally except in patients with a permanent grin, for whom it is more difficult. This early symptom is explained by an increase in tone of the facial muscles. According to the patient the face may remain impassive or be lit by a benign smile. This characteristic appearance is quite often interrupted by spasmodic laughs. When a number of patients are gathered together, this laughing spreads infectiously, mostly evoked by trivialities and quite disproportionate to the events or motions provoking it. Spasmodic weeping has been encountered only exceptionally, most of the patients being more often in a perpetual state of euphoria. Nevertheless, about a third weep spasmodically during questioning.

There is also a certain clumsiness in movements, more especially those of the upper limbs. Movements are more or less markedly slowed and become uncertain. This is particularly striking in occupational movements. Thus with a miner at the face, one finds an increase in the number of working accidents, such as the loss of fingers, while others complain of their difficulty in drinking and in eating their food. Tremor is not the cause, but clumsiness. To this is generally added a marked hyperemotionalism. Without there being any question of imitation, and quite involuntarily, these patients exaggerate their ailments once they are observed. Hyperemotionalism continues to develop throughout the disease.

Certain movements become more difficult to perform: to climb or descend ladders, to lift weights, to sit down on the ground without falling over backwards, as well as getting up again. A gentle push from in front causes loss of balance and a fall. Walking may still be perfectly normal, except when swinging the arms. The first difficulties occur walking down hill, walking on narrow bases such as walls, and in the half-turn. Running soon becomes impossible. Walking backwards is more difficult and in some cases is accompanied by retropulsion and loss of balance.

One also finds adiodokinesis. Neurological examination shows nothing specific except a certain exaggeration of reflexes in the lower limbs. The disorders of the intermediate period have been classified in Table 4 in order of frequency.

TABLE 4

DISORDERS OF THE INTERMEDIATE PERIOD

Clumsiness of movement	82%
Exaggeration of reflexes in lower limbs	74%
Hyperemotionalism	71%
Speech disorders	70%
Masque manganique	65%
Spasmodic laughter	47%
Difficulty in certain movements	45%
Spasmodic tears	32%
Adiodokinesis	30%

The Established Phase.—Generally in a few months the evolution of the disease manifests itself by an aggravation of both subjective and objective symptoms as well as by the appearance of disorders of walking.

At this stage muscular hypertonia in extension is undoubtedly the essential symptom dominating the clinical picture. It is almost always marked in the lower limbs and face and is constant in the sense that it never completely relaxes, but it may be intensified either spontaneously or during movement. Hypertonia is expressed as muscular rigidity, which is seen as a characteristically slow, spasmodic, staggering and sometimes high stepping or swinging gait (Fig. 1). The patient starts with his trunk bent forward as though he were trying to drag his feet from the ground. The steps are short and hesitant. He moves with legs spread apart and knees stretched. Sometimes the feet seem to be flung forward, the toe describing a half-circle at each step. Eventually the patient is able to progress normally by putting his feet flat on the ground. In the majority of cases purchase is obtained with the ball of the foot, and this is the gait named "*Hahnetritt*" or "*pas du coq*" by Von Jaksch (1907) (Fig. 2). Only rarely is the contact made along the external border of the foot. Some patients are able to progress only when supported by another or with a stick (Fig. 3). The staggering so often seen does not appear to be of cerebellar origin but rather due to hypertonia which, slowing down the automatic movements conserving balance, obliges the patient to walk with straddled legs. Walking backwards is impossible, the patient who attempts it falling backwards at once or after a few steps. Climbing up or descending a ladder has long since had to be abandoned, and it is often impossible to maintain balance standing upright with feet together.

The half-turn becomes progressively more difficult, the patient achieving it by little steps, very slowly. In certain cases it becomes impossible, the sick man losing his balance and falling. Walking on uneven ground, and especially on hills, is a source of frequent falls. If it is found possible to climb a stair by the aid of banisters and successive tractions on the legs, going down is virtually impossible. The patient sits down and lets himself slide from step to step.

In those whose muscular power remains intact lifting even light weights from the ground is impossible since once the weight moves the subject loses his balance and falls forward.

In a general way even an extremely light push backwards makes the patient topple over in spite of the angles of support having been strengthened by straddling his legs. Crouching usually leads to falling backwards, the patient being able to rise again only with difficulty.

Most voluntary gestures are carried out very slowly. If they are more or less complex the subject breaks them up, leaving a gap between each. Abnormal tiredness rapidly develops and the patient interrupts his efforts by long periods of rest.

Along with these symptoms, and closely associated with the muscular rigidity, one begins to notice tremors. These may either be spontaneous

FIG. 1.

FIGS. 1 to 3. These photographs illustrate the disorders and peculiar patterns of gait described.

FIG. 2.

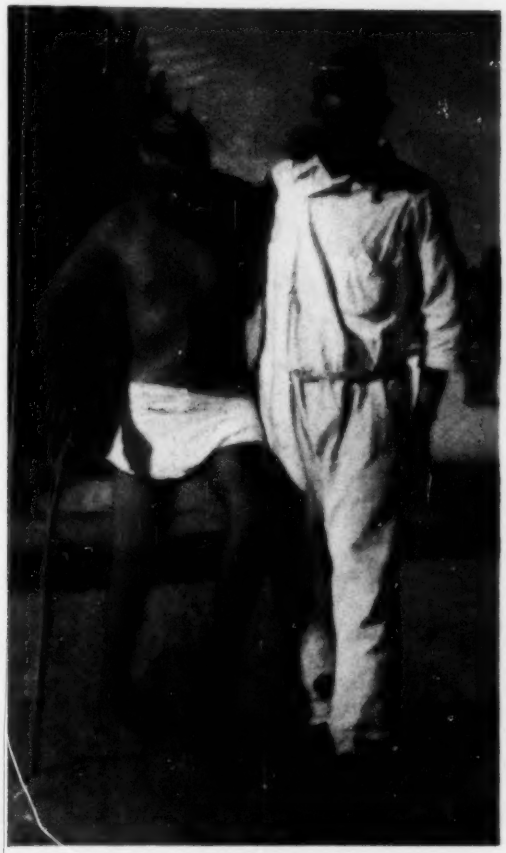


FIG. 3.

(37%) or brought on by fatigue, emotion, or cold (47%). Usually they affect the upper limbs, less often the legs, and are of moderate amplitude and frequency, rhythmic, and regular. Exceptionally generalized shaking may involve the whole body, and affect arms and legs equally.

The low standard of education of the patients has prevented us investigating systematically disturbances of writing. None the less in two of them its irregularity has been studied. Now and then certain words are wholly illegible. The shaky, though at first normally sized, letters become smaller and smaller. From time to time the writer stops to rest and on his resumption the letters are again a normal height (Fig. 4). The symptoms of the onset are at the same time considerably intensified. The fixed expression is still more pronounced and the facial animation that usually accompanies speech vanishes completely. In one case the hypertonia and contraction of the face were such that they led to permanent closure of the mouth ; in another nearly

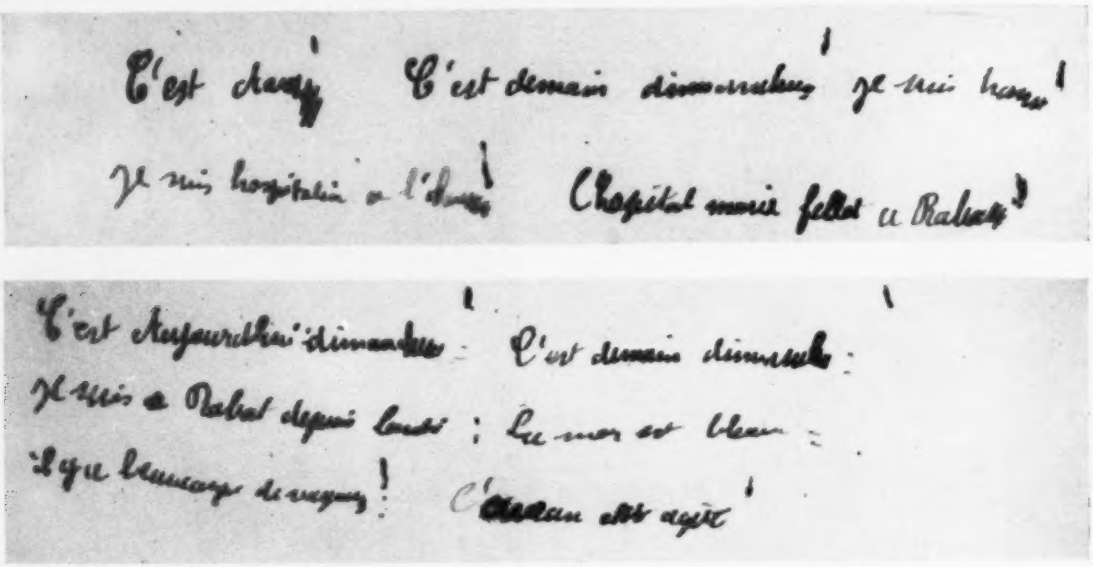


FIG. 4.—Characteristic examples of handwriting showing normal outlines here and there.

permanent occlusion of the eyelids was observed, so much so that they had to be held apart with the fingers so that the patient could see where he was going or to eat. His sight was perfectly preserved.

The spasmodic laughter is more and more frequent, while indifference is complete.

Tranquilly euphoric, the patients display the gravity of their condition without appearing to be affected by it and without putting forward any claims to attention. They complain only of a complete helplessness. Mental disturbances may perhaps be resolved (19%). Loss of memory is exceptional. Sensory functions are intact. Digestive troubles have never been encountered.

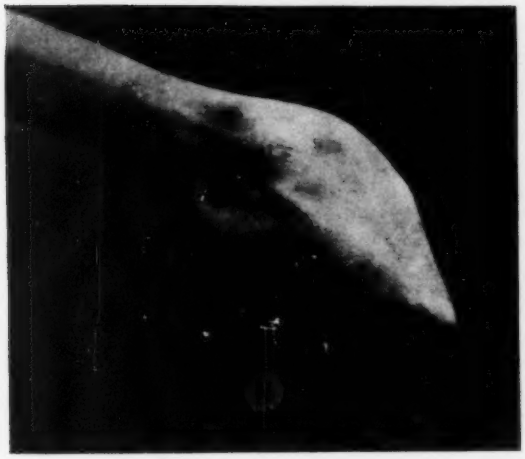
The difficulty in questioning these patients is mainly due to their slowness of speech and to their very great emotionalism.

Disorders of locomotion are met with in all subjects.

A pyramidal syndrome rarely occurs. None the less it must be kept in mind since apart from exaggeration of the tendon reflexes one may elicit some Babinsky responses and foot and patellar clonus. Thirty-nine per cent. of patients present one or more of the three types of emotional disturbance. According to the subject the faculties are blunted, faulty, or absent. Vasomotor and secretory disorders may be encountered, in particular excessive sweating (18%). On the other hand the excessive salivation mentioned by different authors is rare (5%). In spite of the gravity of the neurological signs, the general state of Moroccan patients usually remains excellent. Their musculature is generally conserved. In contrast a certain number of deformities may appear and become permanent. I have seen a case of torticollis fixed by contraction of the left sternomastoid (Fig. 5). Most of the time they are confined to the feet and hands. Exceptionally, clawing of the hands (Fig. 6) and of the toes have been noted. Some other patients have fixed varus deformities with weight bearing on the outer border of the foot. These deformities make walking extremely difficult. Some patients are able to get along only on their knees, others become bedridden. The poisoning develops with varying rapidity and

FIG. 5.—A case of torticollis.

FIG. 6.—Deformities of the hands



establishes itself in varying degrees. Thus graver and less grave forms will be met with, the bedridden type, however, being exceptional.

Development of the Disease

In considering the symptomatology of this condition its progressive character has been seen. Those cases which sometimes recover if they are withdrawn promptly from dangerous work will not be considered but discussion will be confined to those victims in whom the established lesions have caused disability. Table 5 shows the distribution of the degrees of invalidism.

TABLE 5
DEGREES OF INVALIDISM

Degree of Disability	Up to 25%	25–50%	50–75%	75–100%	Needing Support from Another Person
Cases	—	8·6	19·6	67·5	4·3

The degree of disability is on the whole high. Moreover, the disabilities are not definitive, in the sense that they can become worse in the course of years. It is for this reason that legislation allows victims recourse to arbitration in the event of aggravation of their symptoms. In no case must the slowness and tenacity of the progress of the disease be forgotten. It is inexorable: once established it does not regress.

In all the patients examined the nervous disorders showed, after the patient had stopped work, no tendency to regress but I have been notified of two patients with disorders of walking which finally disappeared. These patients have not been found again, and the accuracy of these facts has not been verified. However, certain symptoms can diminish and even disappear, in particular the disorders of speech and the tremors. On the other hand those of walking are not altered. Two patients had ceased to have any contact with manganese, one for three years, the other for four, when their first symptoms appeared.

The explanation of the mechanism of this evolution has been investigated by various authors. I agree with those who think that once manganese gains entry to the body it is eliminated only very slowly. I have, in fact, found in one patient, who had given up his work 17 years before, 72·2 mg. of manganese eliminated per kg. of hair. Another eliminated 254·33 mg. 11 years after stopping work, while in a further example 174·7 mg. per kg. of hair was eliminated two years after stopping work.

We have not been able to determine in which organs the metal is deposited since it has not been possible to perform a necropsy on a victim of this poisoning, but it seems that slowness of elimination allows the disease to develop though the patient is out of all contact with the toxin and thus favours the establishment of progressive and irreversible lesions.

Manganic Pneumopathies

Certain writers (Brezina, 1921; Bubarev, 1931; Baader, 1932; Büttner and Lenz, 1937; and Jötten, 1942) have described pneumonia caused by manganese, and, from the experimental point of view, the remarkable investigations of Lloyd Davies (1946) have defined the role played by manganese in pneumonia.

Lack of time and the necessity of seeing the disease as a whole have prevented us so far from making a detailed study of the problem.

It is not proposed to consider the clinical picture of the pulmonary complications seen among manganese workers but some observations and figures gathered in the course of our studies will be given.

In Morocco Cauvin (1943) had already pointed out during the winter of 1939–40 the importance of the pneumonias and the high death rate associated with them. A comparable incidence did not occur again until 1947, a year which was undoubtedly the worst. Because of difficulties resulting from the war housing and sanitary conditions were deplorable. At once schemes were launched which greatly improved nutrition, housing, and personal hygiene, and since then these serious pulmonary disorders have not been a problem of such magnitude. However, the epidemic led us to suppose that manganese could not be the sole aetiological factor at work. It could, on the other hand, undoubtedly be an aggravating element. Approximately (excluding bronchitis) 3·7% of workers are affected each year with pneumonia and other respiratory diseases with an average morbidity of 11%. Bronchitis, confused as it is with common ailments, does occur frequently among manganese miners.

The clinical signs of manganese pneumonia are at first those of acute alveolar inflammation. The extremely violent character of this condition, which becomes very serious almost at once, may mislead the doctor. Dyspnoea is marked, respiration shallow and gasping. Cough and expectoration are rare. The illness alters, however, after the third day from a frank pneumonia to less well defined localization and discrete pleural involvement. About this time too is seen the characteristic facial cyanosis. A fatal issue may ensue from heart failure between the fifth and the tenth days. It may also occur suddenly in patients regarded as cured. The usual drugs, in particular sulphonamides and antibiotics, mostly are without effect.

We have found specially notable among the few patients whom we have seen with this condition, a leucopenia with relative polynucleosis, an enormous rise in the erythrocyte sedimentation rate (120 in the first hour using a Westergren tube), and eosinophilia in the sputum.

Many investigations are still needed to study this special aspect of manganese poisoning. Unfortunately, the isolation of the mining districts has up to now prevented our getting the usual *x*-ray films and local customs forbid our doing necropsies. Thus it is difficult to be sure whether one is dealing here with an ordinary pulmonary infection complicated and aggravated by manganese, or subacute oedema, the pulmonary manifestation of a toxic state.

Individual Susceptibility

If the number of cases of manganism are related to the number of workers in the mining industry it is seen that the incidence is very low in comparison with the total. This is still more striking when the fluctuating nature of the local pool, which involves a constant inflow of workers, is considered. On the other hand, if it is conceded that only the pulverized ore is liable to produce poisoning the percentage of persons affected is high. (We have tried to establish the statistics but unhappily the lack of registration and the perpetual changes again prevent us from presenting useful figures.)

Apart from subjects showing neurological organic lesions or having previous meningitic or encephalitic conditions, it is difficult to foresee that an individual will tolerate exposure to manganese badly. On the other hand lesions of the excretory system (liver, kidneys) seem important in view of the very slow elimination of manganese by the body. But what appears most interesting, from the point of view of individual susceptibility, is the state of the respiratory tract and more particularly the ability of the pulmonary alveoli to cleanse themselves of manganese dust. If each day the subject manages to get rid of most of the inhaled particles, intoxication will not ensue. It is necessary in some way to balance the intake and output of dust. So long as manganese particles are not got rid of in a satisfactory fashion they are absorbed and will produce irreparable neurological lesions. Unfortunately, this threshold cannot be determined at present either clinically or in the laboratory. In the interests of prophylaxis, therefore, only those with sound pulmonary and nervous systems should be employed as manganese workers.

It has often been suggested that alcoholism and syphilis are of importance in determining individual susceptibility to manganese poisoning. We do not consider these factors of appreciable importance. So far as the former is concerned only one of our patients drank alcohol ; as for the second only 10% gave positive serological reactions. The others had never had any specific treatment.

We tentatively suggest the possible influence of carbon monoxide. Ventilation is often deficient, with the result that carbon monoxide is found in the atmosphere in certain workings. For example we have obtained readings varying from 0·01 per 1,000 to 0·05 per 1,000. While this gas is not in sufficient quantity to produce serious accidents, it may perhaps favour the establishment of neurological lesions by manganese poisoning.

There does not seem to be any bias between the sexes on the incidence of the disease. It is true that underground work, which alone produces poisoning, is forbidden to women. So far as age is concerned (Table 6) it would appear that the critical age for intoxication lies between 30 and 40 years.

TABLE 6
AGE RELATED TO INTOXICATION

Ages	Up to 20 Years	20–25 Years	25–30 Years	30–40 Years	40–50 Years
% sick	0	17·1	27·6	43·5	11·8

This factor cannot be regarded as absolute, since it would be necessary to know the age distribution of the whole labour force, and this is very difficult.

Biological Changes

We have carried out many investigations of sick patients, suspects, and those considered healthy in an attempt to find a test for manganese poisoning. We propose to publish elsewhere the results of this study, which involves more than 10,000 analyses.

While we have not found an absolutely indisputable test, it none the less appears to us that the victims of manganese poisoning display certain changes in the white cell count, the rate of excretion of the 17-ketosteroids, and the basal metabolism.

White Cell Count.—In 52% of patients we found a change in the white cell count with a relative increase of lymphocytes and a decrease in the number of polymorphonuclear cells.

Excretion of 17-Ketosteroids.—There is without question a disturbance, 81% of our patients showing a diminished excretion.

Basal Metabolism.—Employing our usual techniques for measuring basal metabolism we found that it was increased in 57% of cases, often to a very marked degree. Had it been possible for us to use Durupt's effort test in all circumstances this percentage would have been still higher. Most of the patients whom it has been possible to test have given a positive result.

Elimination of Manganese

It is incontestable that, as for other metals, the toxicity of manganese is controlled on the one hand by the ease with which it enters the general circulation and on the other by the gap between absorption and excretion.

All the manganese that penetrates to the general circulation is not integrally fixed. A large part is excreted. The liver, thanks to its detaining power, plays an important role since it excretes manganese in the bile, and so the faeces form the chief route by which it is eliminated. Thus the average quantity of manganese we have estimated in the faeces is 54 mg. per kg. Another route, though less important, is in the hair, and we have recovered in various groups of subjects the following amounts in milligrams of manganese per kilogram of hair :

Apparently healthy subjects ..	365
Suspected subjects	232
Ill subjects	105

Elimination is less in suspects and in the sick than in apparently healthy men. Of course, the sufferers from manganism had mostly been away from work for several years but the suspects were in contact with the ore to the same degree as the apparently healthy. It must therefore be supposed that those affected are more especially those in whom the elimination of manganese is deficient or extremely slow, as we have already seen in connexion with the development of the illness. Urinary excretion plays but a minor part and is found in only about 10% of subjects. Manganese in the urine varies then from 16 to 500 mg. per litre.

Pathogenesis

Manganese gains access to the body by the pulmonary and digestive routes. In our view the latter is not of interest. In fact, apart from jobs where crushing raises a great deal of dust, we have not found manganism even in the washing plant, and yet these workers absorb really large quantities of manganese by mouth and from the hands. Furthermore, we have verified experimentally the lack of toxicity of the metal so ingested. It seems that this may be partly due to the poor absorption of mineral by the body during its passage through the intestine, and perhaps also because particles not absorbed directly after their formation lose most of their toxicity. The pulmonary tract is undoubtedly the major route for penetration and also the only dangerous one. Dusts of less than 5 microns reach the alveoli and are then in contact with phagocytes which, after ingesting them, bring them into the general circulation by means of the lymphatic channels. We have recovered from the sputum some of these cells enclosing manganese particles. Apart from this mode of penetration there is probably some absorption of dust by solution through the alveolar mucosa.

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Some writers, struck by the really negroid appearance of manganese miners, have for this reason tended to attach great significance to cutaneous penetration. Experimental trials with dusting and controls by analyses of manganese in the

tissues have demonstrated that this hypothesis carries no weight.

On no account must the fact be forgotten that the area of the alveolar epithelium represents about 25 times the surface of the skin, and otherwise offers an ideal situation for penetration of the organism by the dusts which come in contact with it during respiration.

Conditions of Toxicity

Among the factors which condition the toxicity of the manganese ore dusts, the chief is certainly the number of particles less than 5 microns in size. To this must be added the content of the dusts in toxic metal and hence the richness of the mineral. This last factor varies a great deal with the type of ore. It also differs according to the mine and even sometimes in individual workings according to the seam.

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From the mineralogical point of view it appears that the most dangerous manganese ore is braunite, and in particular the crushing operation which conditions the toxicity.

The possible activating role played by certain metals or alkaline-earths associated with manganese in the ores must not be forgotten. Lead, which is present in considerable quantity in some deposits, seemed especially interesting. However, despite our researches we have failed to detect any symptoms of lead poisoning among the miners.

In the face of all these elements it is very difficult to lay down exactly what quantity of dust and of mineral is necessary to produce intoxication. It is, however, rather odd to note that while the illness appeared on an average after 18 months of work at Tiouine and four years at Imini, it takes about $13\frac{1}{2}$ years to manifest itself at Bou-Arfa. From a biological point of view the highest grades of manganese are met with at Tiouine and this confirms the importance of the degree of breakdown into fine particles.

Furthermore, it is evident that the longer the exposure to a foul atmosphere the greater the risk of intoxication. To the length of stay in dusty surroundings is also to be added the increase in volume and the number of respiratory movements caused by fatigue and physical effort. The quantity of dust inhaled is thus directly related to the occupation of the worker and the conditions of his environment (temperature, humidity, foul atmosphere).

Too many factors are interwoven for it to be possible to lay down in an exact and absolute manner a limit for atmospheric manganese. Our checks of dusty atmosphere lead us to think that a prophylactic system which would keep the number of particles less than 5 microns down to 1,500 per cubic centimetre of air and the manganese content to 100 milligrams per cubic metre of air would on the whole be satisfactory. Even so, it would not completely eliminate all danger of poisoning ; nor can all the other factors we have successively studied be neglected. To be of value any prophylaxis must be adapted to each type of mining operation and to the ore.

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So far as we know there is no treatment for manganese poisoning when it reaches its established phase, but the usual palliative drugs for rigidity and tremor can be used. We have never, in spite of all our investigations, observed any definite improvement, still less regression of the symptoms. It has been the same with the treatment advised by Charles (1927), based on liver and trials of group B vitamins in small and large doses. Physiotherapy and electrical treatment, admittedly carried out with inadequate means, have been inconclusive.

The only possible treatment is immediately to withdraw from work anyone presenting the first symptoms of intoxication. From that moment the aim must be to rid the system completely of the manganese.

We have tried numerous products experimentally over several years and for a long time these trials proved unfruitful. The discovery of the antitoxic action of calcium versenate on manganese allows us to envisage the use of this substance in occupational poisoning by manganese and its derivatives (Rodier, Mallet, and Rodi, 1954). Indeed calcium versenate provides an interesting means of fixing manganese in a non-toxic and readily excreted form, but its use as a prophylactic can only be regarded as an agent for the elimination of manganese, given at regular intervals in such a fashion as to avoid an accumulation of the metal.

From a therapeutic point of view it is difficult to see how it could be used in patients with established neural lesions since these are irreversible. However, for patients in the early stages of poisoning its action on excretion might perhaps prevent the inexorable evolution of the disease towards total and permanent incapacity.

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tissues have demonstrated that this hypothesis carries no weight.

On no account must the fact be forgotten that the area of the alveolar epithelium represents about 25 times the surface of the skin, and otherwise offers an ideal situation for penetration of the organism by the dusts which come in contact with it during respiration.

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one directing mine-tubs on the same system of medical surveillance.

The organization of the medical service should be directed towards protecting the worker by supervising his state of health from his engagement throughout the course of his employment in the mine.

Examination on First Employment.—This examination aims principally at determining the aptitude of the individual and alloting him to the job which will suit him best. In the case of manganese mines it is wise to exclude from dangerous operations, and in particular those which involve the pulverization of ore, a certain group of subjects whose physical condition leads one to presume that they will tolerate manganese badly.

Those who should be regarded as unsuitable are men with lesions of the excretory organs, the liver and kidneys, blood disorders, organic lesions of the nervous system, progressive pulmonary diseases, and those with a past history of meningeal or encephalitic disturbance. A medical dossier will thus be established for each employee considered suitable for work with manganese.

Periodic Medical Inspections.—The gravity of manganese poisoning demands in effect a detection of pre-manganism so that irreversible neurological manifestations may be avoided. The time that elapses between first contact with the metal and the appearance of neural lesions is of varying length. During this latent period it is reasonable to suppose that functional disturbances may precede organic lesions. The demonstration of such disorders would constitute an excellent clue to pre-manganism. Unfortunately in spite of our researches we have not been able to discover an absolutely specific test for pre-manganism. However, periodic examinations will allow the subjective and objective signs of intoxication to be observed. This examination will be completed as far as possible by certain biological analyses whose importance we have come to recognize in the course of our studies and investigations.

The frequency of these examinations will depend upon the danger of the work. Examinations of rock-drill operators should take place every two months; for other underground workers, ore loaders, conveyors, they should be six-monthly. For the rest of the personnel, and in particular for surface staff, an annual examination should suffice, but from this latter category must be excluded workers who may find themselves in an area where ore is pulverized. For these the same measures should be taken as for rock-drillers.

As well as the usual clinical examinations and the search for early symptoms of intoxication, we advise that particular attention should be paid in the course of routine visits to the following symptoms and tests be carried out :—

In the course of questioning note speech defects and look for diminution or absence of expression and at the same time notice signs of emotional disturbances. Watch for hypertonia, tremor of the extremities, disorders of equilibrium. On a second occasion submit the man to a series of tests including walking slowly and fast, both forwards and backwards. This test will be completed by walking up hill or, even better, climbing a vertical ladder. A half turn from the halt, and walking; pushing test; trial squatting; search for adiodokinesis (with the marionette test); lifting weights; and in addition, if the general education of the subject permits, a writing test.

A comparative study of the results of these various tests and those of the clinical examination should allow the doctor to make an accurate assessment of the development of poisoning.

Examinations on Resumption of Work.—It is essential if these routine examinations are to be completely efficacious to examine afresh every employee who has stopped work for any reason. Only such an examination can determine if the work may be continued under the usual conditions.

As a consequence of these examinations men presenting the following symptoms of poisoning will have to be considered unfit : fixed facies, speech disorders, accentuation of slowness and clumsiness of movement, exaggeration of tendon reflexes, muscular spasticity, disorders of walking, any objective signs of involvement either of the pyramidal or extra-pyramidal nervous system.

It will be necessary to place under close observation subjects presenting subjective signs of poisoning such as asthenia, somnolence, anorexia, psychical excitement, muscular pains, impotence. The clinical examination must be completed by a white cell count. For such patients it is advisable to determine the basal metabolic rate, to carry out an estimation of the urinary 17-ketosteroids, and of the manganese level in the blood.

In persons presenting with lymphocytosis, a raised basal metabolic rate, diminution in the titre of the urinary 17-ketosteroids, a blood level of manganese of 250 g. ‰ will be regarded as suspect.

If clinical signs and biological changes are found in the same patient the examinations will be repeated at an early date (within 30 days). If the signs become accentuated the man will be considered unfit

Unfitness for work liable to expose the individual to manganese poisoning is not necessarily unfitness for all other work. It is the duty of the employer and the medical service to examine all possibilities of re-employment in the company or out of it each time a change of employment becomes essential.

Technical Measures.—To carry out good prophylaxis against manganism it is very important to recognize that the operation which is dangerous above all others is crushing ore. This is the origin of almost all cases of poisoning.

So far as actual mining of the ore is concerned, the boring of charge holes and blasting are the operations causing most of the dangerous dusts. These two procedures give rise to clouds of dust of very different density and difficult to measure. In general, once the cloud is produced each particle is propelled at its own speed according to its diameter, its weight, and the draughts in the galleries. The danger from these particles will thus depend on the distance of the worker from the source of production. The risks run by underground workers other than those at the drilling or blasting points will therefore be variable and in practice very difficult to determine.

In the mines studied, boring blast holes is done dry with a pneumatic drill, and very rarely with hand-spike and sledge hammer. In the course of boring the quantity of dust emitted depends on the state of the rock, the fine dusts being increased by the hardness of the ore and diminished by moisture (our studies of dustiness in Table 7 demonstrate the importance of this particular factor in the rocky type of ore fairly rich in silica) ; the slant of the bore-hole ; the rapidity with which it is bored ; the escape of air from the drill which produces and maintains a truly artificial dust cloud.

Blasting we have classed among the greatest producers of dust and is particularly dangerous since it is the origin of numerous very fine particles. These are of high toxicity, for they sediment badly and remain in suspension for a long time in the air. We insist on the absolute necessity of shot firing at the end of the shift, and only once at a time. At the same time a substantial gap should be left between the departure of the first shift workers and the arrival of those of the next shift. If ventilation is not sufficient to evacuate the dusts and gas products of the explosion, as often happens in blind-end face workings, it must be supplemented by forced ventilation.

So far as ore cutting with hand drills, as principally used in mines with friable ore, is concerned, this method of exploitation undoubtedly presents less danger. However, according to the amount of dust produced, all danger cannot be completely eliminated, and here also ventilation will speed up the evacuation of dust.

Individual Protection.—It is customary when dusts and their dangers come up for discussion in a mining company to propose at once the use of a mask. Certainly it is sometimes impossible to clear an atmosphere of dust completely and it is only in this instance that one needs to consider using masks. In spite of the refinements which have been incorporated in some models, either in the improvement of air filtration or in lessening the discomfort caused to workmen, their use does not provide a sufficient guarantee of protection to manganese miners. It is only necessary to have followed the work in a mine gallery to know that a mask cannot be kept on during prolonged hewing and shovelling. Although the resistance of the respirator may be as slight as possible, each breath constitutes an effort for the worker, especially in the underground atmosphere where the temperature is considerable and the degree of humidity high. Respiration taking place by lowering pressure, the masks are not absolutely impervious to dusts. Finally manganese ore sticks together and adheres readily. Under the influence of exhaled water vapour, the filter plate soon gets clogged with the collection of dust ; respiration then becomes very difficult and the miner takes off his mask in a foul atmosphere.

We do not intend to reject out of hand the use of the mask as a means of prophylaxis. We would, however, wish that its use would not be considered until all other prophylactic measures have been found to be impossible. The choice of mask must not then be left to the administrative staff. It is necessary to choose something light, solid, and easily held in place and maintained. It should have a pre-filter that is easy to clean, and be furnished with an efficient disposable filter, interchangeable and non-hygroscopic. Masks using a sponge or any kind of pack impregnated with water are illusory. It is essential that the employer should make special provision for the upkeep of these masks. They must be inspected as often as possible in rotation and not simply distributed once and for all in the first place together with lamp, helmet, and boots.

Collective Protection.—In view of the difficulties of individual protection by masks, one sees the necessity of trying to eliminate dust at its origin, and more particularly at the drilling which is the most important source of dustiness. During dry boring

with a pneumatic rock-drill, and apart from the pulverization of the ore, the miner is accustomed to clear the bore-holes with a jet of compressed air. This violent gush of air puts numerous particles into suspension in the atmosphere producing massive dust clouds in ill-ventilated places. Against this, the only efficacious measure is the employment of pneumatic rock-drills with water injection. It is only recently that we have been able to get these progressively introduced in certain workings. The difficulty involved in bringing up a water supply may be simplified by the use of water tanks mounted on mine-tubs. As the manganese beds are found in desert and pre-Saharan regions, it follows that difficulties in supplying water are sometimes insurmountable. The pumping-out of the mine seepage may in such instances provide an extremely valuable source of water.

Good damping of the dust can only be obtained after a sufficiently long contact of water with the ore, and demands a sufficient flow. Different types of pneumatic rock-drills with water injection are on the market and vary in the efficiency with which they eliminate. It again follows that company management should not choose their equipment except after carrying out varying tests or after having gained sound advice. However, water injection is not without some drawbacks. The worker using the apparatus is liable to get wet, especially at the beginning of boring since then the water has a tendency to splash back. In this event the miner has the unfortunate habit of beginning the bore-hole dry. Most of the time we have noticed that the inefficiency attributed to water injection is due either to this mistaken manoeuvre or to the workman, neglectful of the danger of poisoning, reducing or suppressing the flow. Another drawback of water injection is that it raises the humidity of the air and so makes work more difficult in a hot atmosphere. Despite all these drawbacks, this technique remains a very good means of combating dust and seems to be the most efficacious way of limiting manganese poisoning in the mines. In the event of there being no water, it will be necessary to resort to dust traps. Unfortunately, quite often in these devices the interception is inadequate and filtration even less efficient, for they allow a portion of very dangerous dust to pass.

All these measures directly applicable to the source of the particles need to be completed by general arrangements concerning evacuation of dust and general ventilation. Dust arising from shovelling, loading, and blasting can only be removed by a collecting system involving a gathering point, a channel without any inert zones, and eventually a point of discharge of the dust to the air. In spite of everything a good evacuation of dust still leaves a lot of particles in suspension, does not get rid of toxic gases, and does not replace the air. It is, therefore, necessary to complete the cleansing of the working by ventilation. This will have to be adapted to the mine in such a fashion as to avoid eddies which would be the cause of new dust clouds. The use of flexible ventilating pipes, less heavy and easier to manipulate than rigid tubes, appears to be recommended.

General Measures.—We have seen that manganese mostly penetrates by the pulmonary route. In underground work the physical effort needed is very great. It is rendered more difficult by the temperature, the humidity, and the foul air. The number of respiratory movements increase and tend to accentuate the risks of poisoning by raising the quantity of dust entering the body. It is therefore necessary to mechanize as much as possible the handling of ore generating toxic dusts.

The use of " pushers " for blocking-up the rock-drills and so avoiding great physical effort on the part of the miners seems to be a measure to be developed.

Concerning surface installations, it is absolutely indispensable to isolate from other operations the crushing of the ore and pneumatic washing which are both great producers of dust. To the greatest degree possible these processes should be carried out in closed and air-tight installations.

In order to ensure the full efficiency of these measures every company will be concerned to see that a technician is specially charged to check up on various anti-dust appliances. He will also have to ensure strict control of dustiness in the workings.

Finally a progressive organization will promote a rotation of personnel in such a way as to bring about a process of disintoxication by changes of duty. This is very important for rock-drill operators.

But all these measures will be merely speculative if each worker is not told of the dangers of poisoning and if management is not vigilant to see that the preventive means put at the workman's disposal are effectively used.

Compensation Legislation

Following the example of a number of countries, such as Great Britain, Germany, Chili, Switzerland, and the U.S.S.R., Morocco has listed manganese poisoning among the compensatable occupational diseases.

This legislation recognizes among the manifestations of manganese poisoning the nervous

syndrome and pneumonia. It defines the work liable to produce it as the extraction, handling, and industrial use of the ores. This legislation is still not complete and will require recasting upon certain points. As a result of our researches we are studying at present a full text which will define the conditions of compensatory action, the medical measures to be applied in mines, and the prophylaxis to be instituted there.

It seems important to point out that the period of one year laid down under certain laws after which responsibility lapses is quite insufficient. We have seen a certain number of cases appear several years after stopping work, and it therefore seems reasonable that the period of responsibility should extend for five years. Legislation should also allow a plaintiff to obtain a revision of his pension in the event of his symptoms worsening. It is in fact known that a small percentage disability evolves more or less rapidly to a 100% incapacity.

Summary

This paper surveys recent knowledge of manganese poisoning among Moroccan miners. After a brief introduction on the manganese deposits where the disease is encountered, the clinical syndrome is described. One hundred and fifty cases of poisoning have provided the material for these investigations. Manganism is studied under its two aspects: the neurological syndrome progressing inexorably and irreversibly, and the pneumopathies. Individual susceptibility, whose role seems important in this condition, and the conditions for toxicity are successively discussed. The latter constitute one of the most difficult problems since prophylaxis depends directly upon it. Some problems, such as the part played by dust, are described. If at present treatment of the disease is only palliative and cannot produce regression of symptoms, the elimination of manganese by the use of calcium versenate opens new possibilities. An important section is devoted to problems of prophylaxis, and exact indications are given of both medical and technical measures to be taken. Finally certain legal aspects of compensation are presented and discussed.

The illustrations in this article belong to the author's collection or are extracted from the film " Manganism " produced by J. Rodier in collaboration with J. Boyer and R. Chenay, the script writer.

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DERMATOSES IN JUTE WORKERS

BY

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Although skin changes in workers associated with the manufacture of various textiles, especially cotton, have been the subject of numerous communications (*e.g.*, Southam, 1927; Brockbank, 1941) there are few references in the literature to dermatoses in jute workers. Henry (1947) refers to one case of scrotal carcinoma in a jute worker out of a total of 1,421 notifications to the Factory Inspectorate. Even the standard textbooks on occupational diseases of the skin (Schwartz, Tulipan, and Peck, 1947; Prosser White, 1934) contain little information on this subject, and a paper on jute dermatitis in Indian workers (Curjel and Acton, 1924) describes only the follicular lesions of oil acne. There has not been, to our knowledge, any comprehensive survey of skin changes in jute workers.

One of us (J. K.) had noted certain changes on the exposed skin of elderly jute workers, and since the major part of jute manufacture in Britain is concentrated in or around Dundee, it seemed that a planned survey in this region would fill a gap in our knowledge and produce results of some value.

This study only refers to skin changes which may be associated with the manufacture of jute from its raw state as received in this country to the finished woven article. The principal difference between the manufacture of jute and that of most other fibres is that jute has to be treated with a mixture or emulsion of oil and water before it can be spun; the jute worker therefore is exposed to an unnaturally oily fibre in addition to any contact with oil used in lubricating the machinery. Up till about 25 years ago whale oil was used but since then varying proportions of mineral oil have been added and whale oil has been used less and less until the recent war years when its scarcity and high price stopped its use altogether. The oil is added to the jute fibre in the first stage of manufacture (known as "batching") when it is softened between rollers. It is then "prepared" by a carding process similar to that used in the cotton and woollen industry; the "sliver" ribbon then goes through the "drawing" department in which it is thinned and elongated and is then "twisted" on to bobbins ready for spinning. Jute spinning, unlike cotton spinning, is done on frames with spindles revolving at the high speed of some 4,000 revolutions per minute. The spun yarn is wound either for the warp ("spool-winding") or for the weft ("cop-winding") and the "beamers" make the warp thread ready for the weavers. Woven jute is coarse material, used for a variety of purposes such as sacks or backing for linoleum. The woven cloth may be taken to the "sewing flat" for conversion into sacks or to the "calender" where it is folded, rot-proofed if need be, and otherwise prepared for the market. In one establishment we visited there was a tar house in which jute yarn was coated with tar for a special purpose. Terms used for other workers are self-explanatory. All had contact with jute except the office and canteen staffs.

Our investigation was divided into two main parts: (1) a clinical survey covering a period of one year (July, 1952 to August, 1953) of all new patients over the age of 16 attending the ordinary skin out-patients clinic of Dundee Royal Infirmary, the only centre for such clinics in the city; and (2) a field survey of all workers in seven jute mills and factories in the city.

Clinical Survey

The records were divided into three groups: (A) patients whose skin conditions were considered by us to be due to their present or past employment as jute workers; (B) patients who were or who had at any time been jute workers but who attended for skin conditions considered to have no connexion with such work; and (C) patients who had never been jute workers.

There are in Dundee (population about 180,000)

17,800 employed jute workers (7,600 men and 10,200 women). An estimate cannot be given of the numbers of local inhabitants who at some time or another have worked with jute.

The conditions found in Group A could be readily classified under three headings : (1) dermatitis of contact or infective origin, (2) oil acne, and (3) malignant or pre-malignant changes of the skin.

Table I correlates these dermatoses of jute workers with their sex, age, and mean years of employment in jute works.

TABLE I
RESULTS OF CLINICAL SURVEY OF DERMATOSES OF JUTE WORKERS

Dermatosis	Total	Male	Female	Mean Age in Years	Mean Years in Jute Industry
Dermatitis (contact or infective)	16	6	10	46·6	18·9
Oil acne	5	4	1	26·6	4·4
Pre-malignant or malignant changes	10	4	6	71·3	42·8
Total	31	14	17		

Dermatitis (Contact or Infective).—Sixteen patients, six men and 10 women, suffered from dermatitis but in no case was sensitization to jute itself proved by patch-testing. Seven women had dermatitis of the hands and forearms apparently due to friction from the rough jute aggravated by oil and dirt. Of the remaining three women, one had a contact dermatitis clearly due to disinfectant used in cleaning lavatories and another a contact eruption due to medicaments applied to a minor injury. A third, who had a previous history of contact dermatitis when working in a hat factory, developed dermatitis while collecting jute waste and rags.

Of the six cases of dermatitis in men, three were attributed to medicaments applied to minor injuries, one was caused by paraffin used in cleaning machinery, and another by a rot-proofing solution. The remaining man had an infective dermatitis of the hands and had previously suffered from seborrhoeic dermatitis of the scalp.

Oil Acne.—It is popularly considered that oil acne is an inevitable occurrence at some time or other in jute workers and it is disregarded unless severe in degree or infected. Only five patients, four men and one woman, required treatment at the Skin Department for this condition during the year.

Two male patients (batchers), whose clothing became saturated with oil, had oil acne affecting the arms, legs, and genital region. One man had, in addition to oil acne of the forearms, a severe acne vulgaris of the back and chest and the fourth man exhibited marked peri-orbital comedone formation. The single female case occurred in a young weaver and the lesions were confined to the forearms.

Pre-malignant and Malignant Changes.—The malignant and pre-malignant conditions found in the 10 patients shown in Table 2 require more detailed consideration because they have not hitherto been considered occupational hazards among jute workers. It will be noted that all six female patients were, or had been, jute spinners ; two of them had had multiple carcinomata. The four men had been in more varied types of employment in jute works ; in two cases the site of the carcinoma was the scrotum. Of the 10, eight showed degenerative changes of the skin such as atrophy, pigmentation (dark, patchy and readily distinguishable from freckles), keratoses, purpura, and telangiectases affecting the face, forearms, and hands. Such changes have been apparently regarded

TABLE 2
MALIGNANT AND PRE-MALIGNANT CONDITIONS IN JUTE WORKERS

Case No.	Age	Sex	Years in Jute Industry	Occupation	Diagnosis	Skin Changes	Site of Epithelioma
1	81	F	58	Spinner	Keratoses	A Pig K*	Has had several facial carcinomata removed
2	60	F	40	Spinner	Epithelioma	A Pig K C T	L. hand ; had previous epithelioma L. forearm
3	62	F	49	Spinner	Epithelioma	A Pig K C	Intradermal carcinoma R. forearm
4	78	F	37	Spinner	Epithelioma	A Pig K C Pu T	R. forearm
5	80	F	50	Spinner	Epithelioma	A Pig K C Pu	R. forehead
6	90	F	22	Spinner	Epithelioma	A Pig K C	R. forearm
7	88	M	52	Batcher	Epithelioma	C	Arm
8	51	M	34	Batcher	Keratoses	Pig K FP	Epithelioma of scrotum in 1950
9	49	M	32	Foreman spinner	Epithelioma	C	Scrotum
10	74	M	54	Maintenance engineer	Epithelioma	A Pig K C	Face

*A = atrophy, Pig = pigmentation, K = keratoses, C = carcinoma, Pu = purpura, T = telangiectases, FP = follicular plugging.

as more or less normal senile changes and one of the main objects of our investigation was to find out whether or not they are connected with employment in jute works and, if so, why they occur. Similar changes were found in 60 (20·2%) of 297 patients who were or had been jute workers (groups A and B), while of the 466 patients in Group C not employed in the jute industry, only 23 (4·9%) showed such changes. Of these, 19 had been engaged in outdoor occupations with exposure to the sun and four had, in addition, history of exposure to other carcinogenic agents, three being engineers and one a gas worker. It is interesting to note that the Chief Inspector of Factories (1954) in his annual report for 1952 attributes an average of 28 cases of carcinoma per annum in Britain to exposure to mineral oil during the years 1948–52. Our finding of eight cases of carcinoma during the year under review suggests that such lesions have not hitherto been attributed to mineral oil in the jute industry.

The remainder of our investigation was therefore devoted to a study of oil acne and degenerative (pre-malignant) changes.

Field Survey

The fact that such changes are almost entirely confined to the face, neck, forearms, and hands made investigation easy and a large number of workers could be readily examined without interfering with their work. The seven jute firms visited were selected from those which offered us facilities as being examples of establishments of different sizes situated in various parts of the city.

Table 3 shows a summary of the findings in 3,023 employees examined. An unexpected finding was that the occurrence of degenerative changes in the skin was more widespread than had been anticipated, being found amongst workers in all departments except those in canteens and offices. It must be stated, however, that the degree of change was in most cases slight ; spinners undoubtedly showed the most marked changes and, another unexpected

TABLE 3

FIELD SURVEY OF SEVEN JUTE FIRMS SHOWING NUMBERS, MEAN AGE, EXPOSURE YEARS, AND CLINICAL SKIN CHANGES OF EMPLOYEES IN EACH DEPARTMENT

Department	Nos.	Mean Age in Years	Mean No. Years' Exposure	Pre-malignant Changes	Oil Acne	Both Changes	No Changes
Batching	95	43·3	16·8	7 (7·4%)	32 (33·7%)	1 (1·1%)	55 (57·8%)
Preparing	331	41·6	16·3	25 (7·6%)	92 (27·7%)	1 (0·3%)	213 (64·4%)
Spinning	309	39·6	18·0	49 (15·9%)	40 (12·9%)	—	220 (71·2%)
Winding	219	42·0	19·9	21 (9·6%)	34 (15·5%)	1 (0·5%)	163 (74·4%)
Dressing	90	42·0	15·5	5 (5·6%)	14 (15·5%)	—	71 (78·9%)
Weaving	1,184	37·3	16·2	85 (7·2%)	176 (14·9%)	—	923 (77·9%)
Sewing flat	79	31·9	10·1	1 (1·3%)	6 (7·6%)	—	72 (91·1%)
Calender and lapping	267	43·9	16·8	18 (6·8%)	30 (11·2%)	—	219 (82·0%)
Warehouse	10	38·2	16·9	—	3 (30·0%)	—	7 (70·0%)
Transport	19	45·5	16·8	1 (5·3%)	2 (10·5%)	—	16 (84·2%)
Tar house	8	42·0	9·5	1 (12·5%)	1 (12·5%)	—	6 (75·0%)
Mechanics	257	44·2	15·1	6 (2·3%)	35 (13·6%)	5 (2·0%)	211 (82·1%)
Electricians	6	34·3	9·5	—	—	—	6 (100%)
Office staff	130	31·6	11·5	—	—	—	130 (100%)
Canteen staff	19	42·6	5·2	—	—	—	19 (100%)
Total	3,023	39·6	16·2	219 (7·2%)	465 (15·4%)	8 (0·3%)	2,331 (77·1%)

TABLE 4

OIL ACNE AND PRE-MALIGNANT CHANGES IN JUTE WORKERS IN ALL DEPARTMENTS

Age Groups	15–24 years	25–44 years	45–59 years	60+ years	Total
Males					
Normal	146 (70·2%)	295 (71·9%)	282 (74·8%)	125 (82·8%)	848
Oil acne	62 (29·8%)	111 (27·1%)	73 (19·4%)	11 (7·3%)	257
Pre-malignant changes	—	4 (1·0%)	17 (4·5%)	14 (9·3%)	35
Both changes	—	—	5 (1·3%)	1 (0·6%)	6
Total	208	410	377	151	1,146
Females					
Normal	310 (76·7%)	684 (86·7%)	446 (77·9%)	43 (38·4%)	1,483
Oil acne	94 (23·3%)	80 (10·1%)	33 (5·8%)	1 (0·9%)	208
Pre-malignant changes	—	25 (3·2%)	92 (16·1%)	67 (59·8%)	184
Both changes	—	—	1 (0·2%)	1 (0·9%)	2
	404	789	572	112	1,877
Total	612	1,199	949	263	3,023

finding, cop-winders also showed marked degenerative changes, although spool-winders were not unduly affected.

Table 4 shows the incidence of oil acne and pre-malignant changes in all male and female jute workers according to age groups, while Fig. 1 expresses these findings graphically for men and women. Men are more frequently affected by oil acne than women but the reverse is true of pre-malignant changes, and while oil acne is less frequently found in the higher age groups, pre-malig-

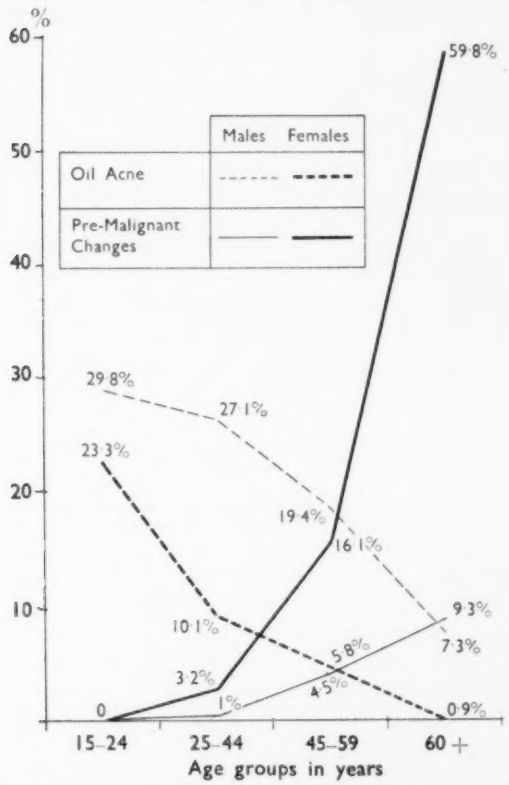


FIG. 1.—The percentage of oil acne and pre-malignant changes observed in 3,023 jute workers in different age groups (see Table 4).

nant changes increase in frequency with age, especially in women. It is a striking fact that in only eight instances were oil acne and pre-malignant changes found in the same person and five of these were elderly mechanics whose work with machinery had brought them especially in contact with oil. Neither the degree of contact with oil nor the skin changes obviously due to oil appear to explain entirely these pre-malignant changes.

The degree of pre-malignant changes amongst spinners and their apparent proneness to develop

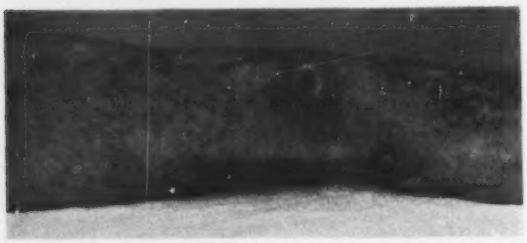
FIG. 2.—Jute spinner aged 62 showing moderate pre-malignant changes (Case No. 3, Table 2).

carcinomata call for further examination of the figures for the spinning department.

Three photographs of typical changes found in spinners are shown in Figs. 2, 3, and 4. These are so

FIG. 3.—Ex-jute spinner aged 81 showing marked pre-malignant changes (Case No. 1, Table 2).

FIG. 4.—Wrist of female ex-jute spinner aged 75 showing pre-malignant changes and an epithelioma.



recognizable that in general hospital wards amongst patients over 50, spinners can often be readily identified at a glance. The ordinary attitude to such changes was well shown in one establishment visited, where we were shown pensioners of the firm who had happened to call that day to collect their money. Bringing forward the first old lady the works nurse remarked, " Well, this one anyway has nothing wrong with her skin ", but a glance at her face correctly identified her as an old spinner.

Table 5 shows the findings in the workers in the spinning departments. The numbers of men engaged there are small, few of them were actually spinners, and too much cannot be drawn from their findings ; but amongst the women, both spinners and others engaged in this department, the figures for pre-malignant changes are high so that in numbers as well as in degree, female workers in this department were found specially affected by pre-malignant changes.

Table 6 shows a similar table for cop- and spool-winders, all women. While the numbers are smaller than for spinners, statistical appraisal shows that cop-winders are more liable to develop oil acne than spool-winders or female spinners and that both cop-winders and female spinners are more liable to develop pre-malignant changes than spool winders. These differences are difficult to explain but it can be pointed out that both spinning and cop-winding are carried out at high speed and the workers' arms and hands near the rapidly moving machinery can be contaminated by oil thrown off in minute droplets either from the prepared fibre or from the machinery itself.

During this field survey only two cases of dermatitis were detected. A spool winder had a mild

TABLE 5

OIL ACNE AND PRE-MALIGNANT CHANGES IN JUTE WORKERS IN SPINNING DEPARTMENT

Age Groups	15–24 years	25–44 years	45–59 years	60+ years	Total
Males					
Normal	11 (57·9%)	12 (63·2%)	7 (53·8%)	1 (100%)	31 (59·6%)
Oil acne	8 (42·1%)	5 (26·3%)	5 (38·5%)	—	18 (34·6%)
Pre-malignant changes	—	2 (10·5%)	1 (7·7%)	—	3 (5·8%)
Both changes	—	—	—	—	—
Total	19	19	13	1	52
Females					
Normal	20 (87·0%)	116 (81·7%)	49 (66·2%)	4 (22·2%)	189 (73·5%)
Oil acne	3 (13·0%)	18 (12·7%)	1 (1·4%)	—	22 (8·6%)
Pre-malignant changes	—	8 (5·6%)	24 (32·4%)	14 (77·8%)	46 (17·9%)
Both changes	—	—	—	—	—
Total	23	142	74	18	257

TABLE 6

OIL ACNE AND PRE-MALIGNANT CHANGES IN FEMALE WINDERS* DIVIDED INTO COP-WINDERS AND SPOOL-WINDERS

Age Groups	15–24 years	25–44 years	45–59 years	60+ years	Total
Cop-winders					
Normal	6 (66·7%)	19 (57·6%)	16 (51·6%)	—	41 (54·7%)
Oil acne	3 (33·3%)	10 (30·3%)	5 (16·1%)	—	18 (24·0%)
Pre-malignant changes	—	4 (12·1%)	9 (29·0%)	2 (100%)	15 (20·0%)
Both changes	—	—	1 (3·3%)	—	1 (1·3%)
Total	9	33	31	2	75
Spool-winders					
Normal	11 (91·7%)	35 (100%)	24 (82·8%)	1 (50·0%)	71 (91·0%)
Oil acne	1 (8·3%)	—	3 (10·3%)	—	4 (5·1%)
Pre-malignant changes	—	—	2 (6·9%)	1 (50·0%)	3 (3·9%)
Both changes	—	—	—	—	—
Total	12	35	29	2	78

*The above figures refer to winders only and do not include 66 workers engaged in other duties in this department.

TABLE 7

NUMBERS, MEAN AGE, EXPOSURE YEARS, AND CLINICAL SKIN CHANGES OF EMPLOYEES IN EACH DEPARTMENT OF ONE FLAX FIRM

Department	Nos.	Mean Age in Years	Mean No. Years' Exposure	Pre-malignant Changes	Oil Acne	No Changes
Batch-blending	18	38·8	16·1	1 (5·6%)	1 (5·6%)	16 (88·8%)
Preparing	85	38·3	12·3	—	10 (11·8%)	75 (88·2%)
Spinning	78	38·7	15·7	4 (5·1%)	11 (14·1%)	63 (80·8%)
Winding	79	34·3	13·3	2 (2·5%)	2 (2·5%)	75 (95·0%)
Dressing	46	35·1	17·1	1 (2·2%)	5 (10·9%)	40 (86·9%)
Weaving	145	37·4	17·4	6 (4·1%)	14 (9·7%)	125 (86·2%)
Calender & lapping ..	43	42·1	15·4	—	3 (7·0%)	40 (93·0%)
Warehouse	18	43·1	18·4	—	2 (11·1%)	16 (88·9%)
Dye house	5	50·6	23·2	1 (20·0%)	—	4 (80·0%)
Cleaning squad	12	35·0	9·0	—	4 (33·3%)	8 (66·7%)
Mechanics	89	41·7	13·9	2 (2·2%)	15 (16·9%)	72 (80·9%)
Electricians	13	27·6	6·3	—	—	13 (100%)
Joiners	18	43·2	12·2	—	—	18 (100%)
Painters	11	40·1	12·0	—	—	11 (100%)
Office staff	7	24·6	3·9	—	—	7 (100%)
Total	667	38·1	14·7	17 (2·5%)	67 (10·0%)	583 (87·5%)

dermatitis of the backs of the hands which was said to be worse in summer and was probably due to sunlight. A sack machinist had a mild friction dermatitis of the tips of the fingers.

Flax Survey

A certain amount of flax manufacture is carried on in Dundee and the opportunity was taken to visit one of the largest flax works in the city. There is very little movement of workers between flax and jute works so that comparable figures could be obtained for two different textile industries in the same city. The results are shown in Table 7. It should be noted that in this establishment a certain amount of hemp is occasionally manufactured and this is treated with oil emulsion, as is jute; flax requires no added oil in its manufacture.

A comparison between Table 4 and Table 7 shows that the incidence of pre-malignant changes is far less in the flax than in the jute industry. For example, the incidence amongst spinners is 5·1% for flax as against 15·9% for jute, and for the whole industries, 2·5% for flax compared with 7·2% for jute. The flax industry also has a lower incidence of oil acne, 10% as compared with 15·4% in the jute industry. No flax worker showed both changes.

Five workers in the "drawing" department complained of roughness and dryness of the hands after cleaning their machines with paraffin, evidently due to its degreasing action on the skin. Two workers in the preparing department complained of irritation of the skin of the forearms after handling hemp. This was apparently due to the coarse texture of the raw hemp.

Discussion

The results of the survey show that jute workers are especially prone to degenerative changes of the skin on exposed areas. Employees in other industries presented comparatively little evidence of degenerative changes and when such changes were present a potential carcinogen, such as sunlight, oil, or both, could be implicated.

Such degenerative changes on the hands, arms, or face seldom cause danger to life. The carcinomata are of low malignancy, radio-sensitive, and usually at a site where simple excision is possible. Where an existing keratosis progresses to carcinoma while the subject is still at work, the time lost because of treatment is negligible.

Scrotal carcinoma, however, presents a more serious clinical problem. The Cancer Register of the Region (population 400,000) records seven cases during the last four and a half years. Of these, three cases (two of which are mentioned in our survey) occurred in jute workers while two of the remaining cases were exposed to oil and one to tar.

We have found it difficult to estimate how long the workers must be exposed to risk before degenerative skin changes occur. O'Donovan (1929), in a report on cancer of the skin due to occupation, has suggested that 20 years' contact with mineral lubricating oils is necessary for the development of carcinoma. Henry (1947) reports latent periods of four, eight, and nine years following exposure to shale or mineral oil but these latent periods must be regarded as exceptionally short. The fact that the minor degenerative changes are accepted as "normal" by the jute workers makes duration almost impossible to assess. We can, however, point to cases in which the exposure has been in the range of 10 to 15 years before marriage, after which the subjects left the industry. Twenty to thirty years later they can be identified as former spinners

FIG. 4.—Wrist of female ex-jute spinner aged 75 showing pre-malignant changes and an epithelioma.

recognizable that in general hospital wards amongst patients over 50, spinners can often be readily identified at a glance. The ordinary attitude to such changes was well shown in one establishment visited, where we were shown pensioners of the firm who had happened to call that day to collect their money. Bringing forward the first old lady the works nurse remarked, " Well, this one anyway has nothing wrong with her skin ", but a glance at her face correctly identified her as an old spinner.

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Normal	11 (57·9%)	12 (63·2%)	7 (53·8%)	1 (100%)	31 (59·6%)
Oil acne	8 (42·1%)	5 (26·3%)	5 (38·5%)	—	18 (34·6%)
Pre-malignant changes	—	2 (10·5%)	1 (7·7%)	—	3 (5·8%)
Both changes	—	—	—	—	—
Total	19	19	13	1	52
Females					
Normal	20 (87·0%)	116 (81·7%)	49 (66·2%)	4 (22·2%)	189 (73·5%)
Oil acne	3 (13·0%)	18 (12·7%)	1 (1·4%)	—	22 (8·6%)
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Both changes	—	—	—	—	—
Total	23	142	74	18	257

TABLE 6

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Normal	6 (66·7%)	19 (57·6%)	16 (51·6%)	—	41 (54·7%)
Oil acne	3 (33·3%)	10 (30·3%)	5 (16·1%)	—	18 (24·0%)
Pre-malignant changes	—	4 (12·1%)	9 (29·0%)	2 (100%)	15 (20·0%)
Both changes	—	—	1 (3·3%)	—	1 (1·3%)
Total	9	33	31	2	75
Spool-winders					
Normal	11 (91·7%)	35 (100%)	24 (82·8%)	1 (50·0%)	71 (91·0%)
Oil acne	1 (8·3%)	—	3 (10·3%)	—	4 (5·1%)
Pre-malignant changes	—	—	2 (6·9%)	1 (50·0%)	3 (3·9%)
Both changes	—	—	—	—	—
Total	12	35	29	2	78

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Department	Nos.	Mean Age in Years	Mean No. Years' Exposure	Pre-malignant Changes	Oil Acne	No Changes
Batch-blending	18	38·8	16·1	1 (5·6%)	1 (5·6%)	16 (88·8%)
Preparing	85	38·3	12·3	—	10 (11·8%)	75 (88·2%)
Spinning	78	38·7	15·7	4 (5·1%)	11 (14·1%)	63 (80·8%)
Winding	79	34·3	13·3	2 (2·5%)	2 (2·5%)	75 (95·0%)
Dressing	46	35·1	17·1	1 (2·2%)	5 (10·9%)	40 (86·9%)
Weaving	145	37·4	17·4	6 (4·1%)	14 (9·7%)	125 (86·2%)
Calender & lapping ..	43	42·1	15·4	—	3 (7·0%)	40 (93·0%)
Warehouse	18	43·1	18·4	—	2 (11·1%)	16 (88·9%)
Dye house	5	50·6	23·2	1 (20·0%)	—	4 (80·0%)
Cleaning squad	12	35·0	9·0	—	4 (33·3%)	8 (66·7%)
Mechanics	89	41·7	13·9	2 (2·2%)	15 (16·9%)	72 (80·9%)
Electricians	13	27·6	6·3	—	—	13 (100%)
Joiners	18	43·2	12·2	—	—	18 (100%)
Painters	11	40·1	12·0	—	—	11 (100%)
Office staff	7	24·6	3·9	—	—	7 (100%)
Total	667	38·1	14·7	17 (2·5%)	67 (10·0%)	583 (87·5%)

dermatitis of the backs of the hands which was said to be worse in summer and was probably due to sunlight. A sack machinist had a mild friction dermatitis of the tips of the fingers.

Flax Survey

A certain amount of flax manufacture is carried on in Dundee and the opportunity was taken to visit one of the largest flax works in the city. There is very little movement of workers between flax and jute works so that comparable figures could be obtained for two different textile industries in the same city. The results are shown in Table 7. It should be noted that in this establishment a certain amount of hemp is occasionally manufactured and this is treated with oil emulsion, as is jute; flax requires no added oil in its manufacture.

A comparison between Table 4 and Table 7 shows that the incidence of pre-malignant changes is far less in the flax than in the jute industry. For example, the incidence amongst spinners is 5·1% for flax as against 15·9% for jute, and for the whole industries, 2·5% for flax compared with 7·2% for jute. The flax industry also has a lower incidence of oil acne, 10% as compared with 15·4% in the jute industry. No flax worker showed both changes.

Five workers in the "drawing" department complained of roughness and dryness of the hands after cleaning their machines with paraffin, evidently due to its degreasing action on the skin. Two workers in the preparing department complained of irritation of the skin of the forearms after handling hemp. This was apparently due to the coarse texture of the raw hemp.

Discussion

The results of the survey show that jute workers are especially prone to degenerative changes of the skin on exposed areas. Employees in other industries presented comparatively little evidence of degenerative changes and when such changes were present a potential carcinogen, such as sunlight, oil, or both, could be implicated.

Such degenerative changes on the hands, arms, or face seldom cause danger to life. The carcinomata are of low malignancy, radio-sensitive, and usually at a site where simple excision is possible. Where an existing keratosis progresses to carcinoma while the subject is still at work, the time lost because of treatment is negligible.

Scrotal carcinoma, however, presents a more serious clinical problem. The Cancer Register of the Region (population 400,000) records seven cases during the last four and a half years. Of these, three cases (two of which are mentioned in our survey) occurred in jute workers while two of the remaining cases were exposed to oil and one to tar.

We have found it difficult to estimate how long the workers must be exposed to risk before degenerative skin changes occur. O'Donovan (1929), in a report on cancer of the skin due to occupation, has suggested that 20 years' contact with mineral lubricating oils is necessary for the development of carcinoma. Henry (1947) reports latent periods of four, eight, and nine years following exposure to shale or mineral oil but these latent periods must be regarded as exceptionally short. The fact that the minor degenerative changes are accepted as "normal" by the jute workers makes duration almost impossible to assess. We can, however, point to cases in which the exposure has been in the range of 10 to 15 years before marriage, after which the subjects left the industry. Twenty to thirty years later they can be identified as former spinners

by the degenerative changes which are then present.

In the present state of our knowledge it is not possible to say whether batching oil or lubricating oil is responsible; nor can one estimate the part, if any, played by the jute itself. One of us (J. K.) with an experience of 30 years' practice in Dundee, considers that there is no apparent increase in the incidence or severity of these changes during the time that whale oil has been replaced by mineral oil in the "batching" process. In view of the findings of this study, many years must elapse before any change will become clinically apparent. Recent work by Cruickshank and Squire (1950) has demonstrated that similar lesions are found in the exposed skin of engineers who use "cutting oils", and Smiley (1951), in a paper on the skin hazards of ropemaking, mentions keratoses and carcinomata in elderly female workers.

With regard to prevention, the working conditions in the local jute industry have greatly improved in the past few years and this may well lead to a diminution of the incidence of these changes in future. If in fact the nature of the oils used in batching or in lubrication can be proved to be the factor or one of a combination of factors, then it would be pertinent to suggest that substitution of a non-carcinogenic white oil might afford a complete or partial solution. Moreover the use of barrier creams and attention to the method of skin cleansing as suggested by Cruickshank (1948) are obviously important.

Reasonable personal hygiene even at present reduces the morbidity from oil acne to a negligible minimum but the high incidence revealed in the field survey does indicate heavy exposure with inadequate removal after work.

Dermatitis, as we have shown, is a minor hazard in jute workers and when it did occur was not caused by sensitization of the skin to jute though the coarse nature of the fibre was a factor in some cases.

Summary

The results of these investigations indicate :—

(1) That dermatitis is not a serious hazard in the jute industry. We found no evidence of sensitization to jute.

(2) That oil acne is common in jute workers.

(3) That degenerative changes in the exposed skin are common in jute workers, especially elderly female operators, particularly spinners.

(4) That these degenerative changes may progress to squamous cell carcinoma in a few cases.

(5) That isolated cases of carcinoma of the scrotum have been found in male jute workers.

(6) The significance of these findings is discussed and a brief outline of possible preventive measures is given.

We are greatly indebted to the assistance of Dr. T. E. Faulkner, Lecturer in Statistics, Queen's College, Dundee, both in planning this survey and in presenting the results. The field survey would have been impossible without the wholehearted cooperation of management and employees of the works we visited. We therefore gratefully acknowledge the help given by the Jute Spinners' and Manufacturers' Association, by the individual managements of the works we visited, and by the Jute and Flax Workers' Union. We have also to thank for their assistance Dr. R. A. Main, Registrar in Dermatology; Mrs. M. Keith, social worker; Miss Audrey Brinkler, on whom the bulk of the clerical work fell, and Mr. D. L. Stewart, photographic technician to the Skin Department, Dundee Royal Infirmary. Part of the cost of this investigation was met by a grant from the Board of Management, Dundee General Hospitals.

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TALCOSIS OF UNUSUALLY RAPID DEVELOPMENT

BY

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A diagnosis of talcosis, so far as we know, has not until now been made in Greece although this disease was first described by Thorel in 1896. This fact may have been due to the small number of talc workers in Greece, but since Thorel's description of talcosis as a definite clinical entity, pneumoconiosis due to talc has been the subject of investigations by many workers.* In most of the reports the writers were able to show the clinical, pathological, and radiological results of pneumoconiosis due to talc.

The present work is based upon the clinical and radiological findings and studies of pulmonary function in cases of pneumoconiosis due to talc after an uncommonly short exposure, the working conditions in the talc factories concerned, and the chemical composition and physical properties of talc powder.

Case Reports

Case 1.—Th. Mis., aged 38 years, left the army in October, 1950, with a clear chest radiograph and afterwards worked in a talc factory for 24 months without any break in his employment. In the factory he worked on electric mills used for pulverizing pieces of soapstone. He usually worked for eight-hour shifts but sometimes for 16-hour shifts as the factory was open day and night. He said that the air in the factory was always contaminated by a cloud of talc. (This fact was confirmed on inspection.) He did not wear a mask or protective clothing and therefore inhaled large quantities of talc powder. He could remove thick crusts of talc from the mouth and nostrils after some hours' exposure.

There was no family history of disease, and the patient had always been well. He had served in the army for more than four years and repeated preventive examinations never revealed any abnormality.

For six months before admission he had complained of productive cough, mucopurulent sputum, and dyspnoea on exertion. He was compelled to stop work because of his symptoms 24 months after starting employment at the factory. As the result of a chest radiograph he was admitted to hospital in November, 1952, for observation.

In hospital clinical examination of the respiratory system revealed sibilant rhonchi, scattered areas of bronchial breathing, and impaired resonance in both lungs. He was apyrexial but dyspnoeic, especially on exertion, with cyanosis of the extremities. He had a productive cough and the sputum contained small grey bodies composed of talc. All sputum tests were consistently negative for *M. tuberculosis* by direct concentration, culture, and guinea-pig inoculation.

A full blood count was normal.

There was a rise in the sedimentation rate (30 in the first hour, 50 in the second, and 96 in 24 hours by the method of Westergren).

The pulse rate was usually 75 per minute at rest. The blood pressure was 125/80 mm. Hg. The electrocardiogram was normal.

A radiograph in November, 1952, showed numerous nodular shadows in both lungs, confluent in some areas. The general condition of the patient at this time belied the widespread radiological extent of the lesions. A radiograph taken in March, 1953, and all the radiographs and tomograms taken at intervals of one, two, or three months showed that the disease progressed from nodule type to " tumour-like " type of disease (Figs. 1 and 3).

A bronchogram revealed no abnormality (Fig. 2). Angiocardiography showed a spasm at the level of the superior vena cava and abnormal arborization of the pulmonary arteries. Investigation of respiratory function revealed pulmonary insufficiency (Tables 1 and 2).

These findings and the exclusion of any other probable disease enabled us to diagnose pneumoconiosis due to talc.

Case 2.—G. Greg., aged 30 years, was discharged from the army with a clear chest radiograph in 1951. He then began work in a talc mill. After 18 months at this work he complained of paroxysmal cough, mucopurulent sputum, dyspnoea on exertion, loss of weight,

* Sand, ; Cunningham, ; Hayhurst (1915); Zanelli (1931); Haynes (1931); Dreessen (1933); Stüber (1934); Dreessen and Dalla Valle (1935); Merewether (1934, 1939); Middleton (1936); Gardner (1938); Nuck and Szcepanski (1939); Policard (1940); Price and Carpenter (1940); Schulz and Williams (1942); Siegal, Smith, and Greenburg (1943); Sorel, Lasserre, and Salvador (1943); Porro and Levine (1943); Pruvost (1943); Greenburg (1947); Perry (1947); Millman (1947); Parmeggian (1948); Bruusgaard and Skjelbred-Knudsen (1949); McLaughlin, Rogers, and Dunham (1949); Hogue and Mallette (1949); Cavigneaux, Charles, Fuchs, and Tara (1950); Baader (1950).

TABLE 1

BLOOD GAS FINDINGS AFTER EXERCISE AND AT REST IN PRESENT SERIES

Case No.	Arterial Blood Oxygen Content (a, at rest; b, after exercise) (Vol. %)		Arterial Blood CO_2 Content (a, at rest; b, after exercise) (Vol. %)		Arterial Blood Oxygen Saturation (a, at rest; b, after exercise) (%)		Arterial pO_2 (rest, mm./Hg)	Arterial pCO_2 (rest, mm./Hg p = part. pressure)	Amount O_2 Removed from Air Breathed (a, at rest; b, after exercise) (Vol. %)		(a) Alveolar Air Oxygen Content (b) CO_2 Content at Rest (Vol. %)		(a) Alveolar Air Oxygen Content (b) CO_2 Content after Exercise (Vol. %)		(a) Alveolar pO_2 at Rest (mm./Hg) (b) Alveolar pCO_2 at Rest (mm./Hg)		Aeration Gradient (mm./Hg)	Transfer-Gradient (mm./Hg)
	a	b	a	b	a	b			a	b	a	b	a	b	a	b		
1	19·1	16·6	54·77	49·32	87	75·7	68	54	3·73	5·13	11·86	6·2	15·8	4·4	84·56	44·2	65·44	16·56
2	15·4	12·4	48·96	40·79	81	64·7	80	45	3·63	5·33	13·2	6·2	14·6	5·6	94·11	44·2	55·89	14·11
4	20·22	17·5	54	42·3	98	84·9	87	51	4·73	6·73	14·2	5·4	14·2	5·2	101·2	38·5	48·8	14·2
5	18·3	15·77	52·23	45·8	93·8	80·8	85	50	4·23	6·43	14·2	5·4	13·5	5	101·2	38·5	48·8	15·2
6	20·31	17·68	48·67	42·49	93·4	81·3	79	44	3·53	4·73	11·8	7·1	16·2	6·4	84·13	50·6	65·87	5·13
7	16·2	13·8	46·2	36·4	82	73	81	42	4·53	5·13	12·4	6	12·4	4·8	88·42	42·7	61·58	8·42
Normal Values	21·5	21·5	46·7–53	—	96+	96+	95	40	4·5	5·5	14	5·5	—	—	100	40	50	5

TABLE 2

MEASUREMENTS ON VENTILATION IN PRESENT SERIES

Case No. and Stage of Disease	1, III	2, III	3, III	4, II	5, II	6, I	7, I
Vital capacity (ml.)	1,420	1,380	1,700	2,620	2,850	2,800	3,300
Ventilation (l./min./sq. m.):							
At rest (normal value 3–4 l.)	4·7	4·9	4·2	5·8	6·1	5·6	6·0
After exercise (normal value, 8–11 l.)	9·3	8·0	10·2	10·8	12·2	10·7	13·5
M.B.C. (l.)	56·8	27·0	40·0	34·0	32·0	51·0	88·0
Arterial blood oxygen deficits (ml.)	150	140	100	75	60	0	0
Oxygen consumption (ml./min/sq. m.):							
At rest	175	172	130	137	244	253	217
After exercise	477	378	250	726	784	548	719
Duration of dyspnoea after exercise (sec.)	230	190	300	145	120	80	70
Body surface area (sq. m.)	2·23	1·5	1·98	1·9	1·75	1·67	1·96
V.C. decrease from predicted (%)	67·8	64	57·62	43·6	22·0	37·4	18·0
*M.B.C. decrease from predicted (%)	53·9	66·4	62·0	71·0	66·3	50·0	17·7

*Classification according to the description of Pancoast and Pendergrass (1931).

and general weakness. Examination of the respiratory system revealed dullness to percussion in some zones of both lungs and a few sonorous rhonchi and physical signs of emphysema. A radiograph showed bilateral mottling, confluent in some areas, and " tumour-like " appearances (Fig. 4).

All sputum tests, including guinea-pig inoculation, were consistently negative for *M. tuberculosis*. A full blood count showed a slight degree of anaemia. The sedimentation rate was 25 in the first hour, 40 in the second, and 82 by the twenty-fourth hour by the Westergren method.

Functional tests showed pulmonary insufficiency (Tables 1 and 2).

Case 3.—D. Thom., aged 49 years, worked for 60 months in a talc mill. Three years after starting work he complained of dyspnoea on exertion, cough, mucopurulent sputum, and general weakness. He gradually became more cyanosed.

Clinical examination in November, 1952, revealed impaired vesicular breathing in both lungs and bronchial breathing confined to both upper lobes, prolongation of expiration, and sibilant rhonchi. The radiological examination showed extensive " tumour-like " appearances on both lungs and bilateral diaphragmatic pleurisy (Fig. 5). All the sputum tests were consistently negative for *M. tuberculosis*. A full blood count was normal. The sedimentation rate in the first

FIGS. 1 to 6.—Typical radiographs of patients in the present series showing mottling and tumour-like appearances characteristic of talcosis.

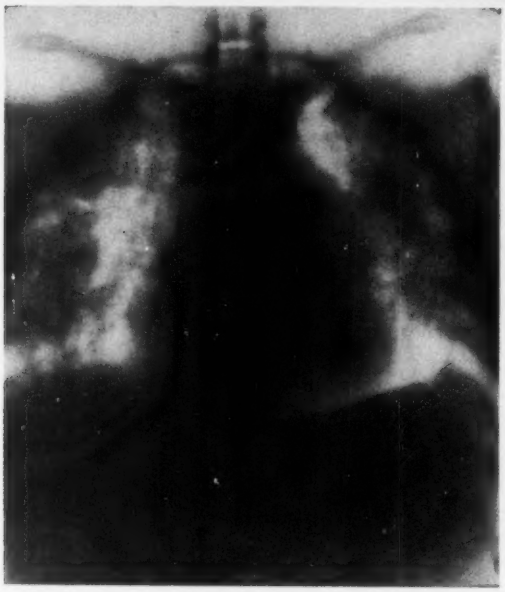

FIG. 1.

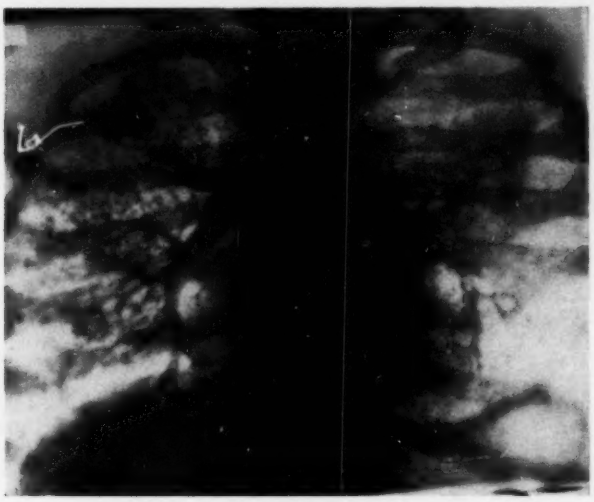

FIG. 2.

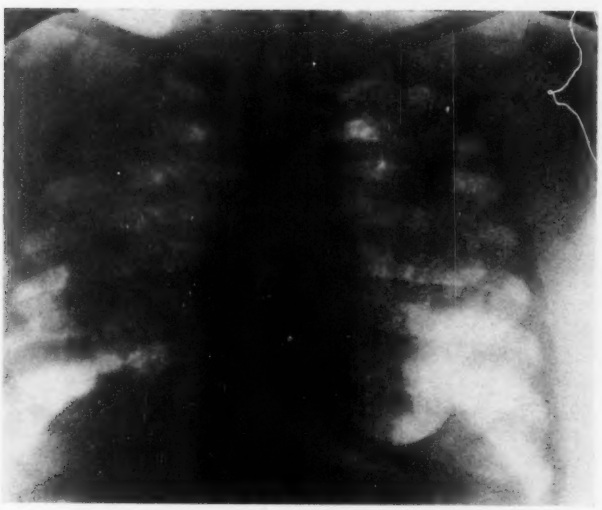

FIG. 3.

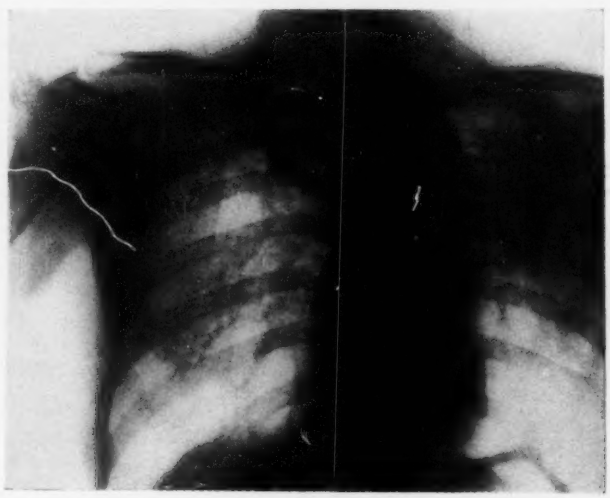

FIG. 4.

FIG. 5.

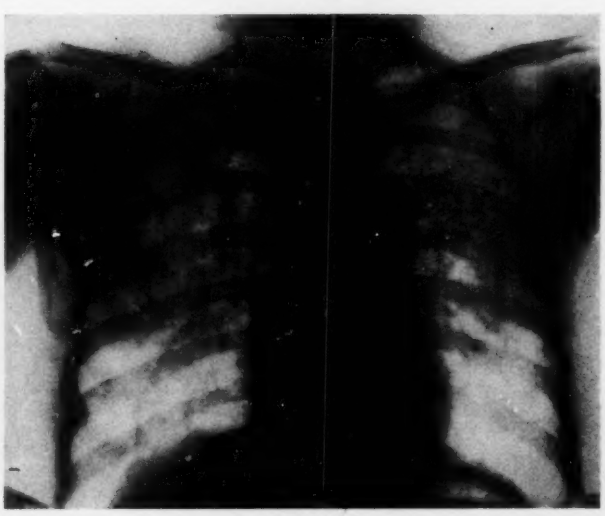

FIG. 6.

hour was 38, in the second hour 70, and 116 by the twenty-fourth hour. Examination of respiratory function showed pulmonary insufficiency (Tables 1 and 2). The patient became worse and died from pulmonary failure in September, 1953. A post-mortem examination was carried out by Dr. Melissinos who reported that extensive massive fibrosis existed in both lungs, especially in the upper lobes. Numerous nodules were found which were confluent in some areas. On microscopic examination no evidence of tuberculosis was found. The pathological diagnosis was pneumoconiosis.*

Case 4.—K. Mak., aged 28 years, worked in a talc mill for 18 months. At the end of this time he complained of persistent cough, dyspnoea on exertion, and mucopurulent sputum, and for these reasons he left the factory. On examination talc particles were found in the sputum. He gradually continued to lose weight and strength. A clinical examination in February, 1953, revealed scattered bronchial breathing and rales in both lungs. The radiograph showed mottling in both lungs, confluent in some areas. All sputum tests were consistently negative for *M. tuberculosis*. A full blood count was normal. The sedimentation rate in the first hour was 16, in the second hour 28, and by the twenty-fourth hour 41. Respiratory function tests showed pulmonary insufficiency (Tables 1 and 2).

Case 5.—N. Chr. was a 22-year-old mill worker who had been in the talc factory for 26 months. After 18 months there he complained of dyspnoea on exertion, cough, and mucopurulent sputum. He gradually lost weight.

Clinical examination in April, 1953, revealed bronchial breathing in the upper lobes and a few sibilant rhonchi. The radiological examination showed mottling in both lungs, confluent in the upper lobes (Fig. 6). All the sputum tests were negative for *M. tuberculosis*. The sedimentation rate in the first hour was 22, in the second hour 36, and by the twenty-fourth hour 72. Pulmonary function studies showed impaired function (Tables 1 and 2).

Case 6.—S. Sof. was a 35-year-old mill worker who had been in the talc factory for 22 months. Symptoms began 18 months after starting work in the factory. He complained of gradually increasing dyspnoea of effort, paroxysmal cough, and expectoration. Bodies made of talc were found in the sputum.

Clinical examination in April, 1953, revealed scattered areas of bronchial breathing and rales in both lungs. All sputum tests were consistently negative for *M. tuberculosis*. The chest radiograph revealed bilateral mottling especially in the right lung. The sedimentation rate in the first hour was 18, in the second hour 25, and in the twenty-fourth hour 42.

Pulmonary function was impaired (Tables 1 and 2).

Case 7.—G. Phr. was a 42-year-old mill mechanic who had been in the talc factory for 40 months. Symptoms began 28 months after starting work in the factory when cough with a small amount of sputum and slight dyspnoea of effort appeared.

Clinical examination in January, 1953, revealed no abnormality. The chest radiograph showed reticulation and scattered mottling in both lungs. All sputum tests were consistently negative for *M. tuberculosis*. The sedimentation rate in the first hour was 14, in the second hour 28, and by the twenty-fourth hour 36.

Pulmonary function was impaired (Tables 1 and 2).

Case 8.—S. Les. was a 38-year-old mill worker who had been in the talc factory for 16 months. He first experienced symptoms a few months before examination with the onset of dyspnoea on exertion, cough, and mucopurulent expectoration.

Clinical examination in June, 1953, revealed bronchial breathing in the upper lobes and a few sibilant rhonchi. The chest radiograph showed reticulation and confluent mottling in both lungs All sputum tests were consistently negative for *M. tuberculosis*. The blood sedimentation rate in the first hour was 15, in the second hour 24, and by the twenty-fourth hour 42.

All the cases appeared by clinical, radiological, and laboratory examinations to be pneumoconiosis due to talc developing after an uncommonly short interval of exposure. The condition may have been due to the unusually irritating effect of inhalation of talc powder and to unhygienic working conditions.

Conditions in Talc Factories

The patients described above were working in either one or the other of the two talc factories in the Piraeus. One of these factories, that at Alav, obtained its raw material from the island of Tinos, the other, at Eviex, from the mountain Hymetos. The factories are old buildings, poorly ventilated, without any system of air conditioning. A permanent cloud of talc particles permeates the air. The workers remain in this atmosphere for eight-hour shifts, some of them working 16-hour shifts, as both factories are open day and night. Some of the workers, who slept on the premises near the mills, were exposed to a talc-laden atmosphere during sleep.

The manufacture of talc in these factories consists in breaking the raw material, soapstone, into smaller pieces by machinery or by hand. The smaller pieces are pulverized or powdered by an electric mill and the powder is then shovelled into sacks by collectors.

The employees do not wear masks or protective clothing and therefore inhale large quantities of talc powder and after some hours' exposure can remove thick crusts of talc from the mouth and nostrils. All the workers alternated on the different stages of the work.

* The pathological findings will be reported separately in detail by Dr. Melissinos.

All lighting is artificial as daylight cannot enter through the closed doors and windows.

There are no recreation rooms or bathing facilities for the workers and they spend their rest periods in the same atmosphere as that in which they work.

The concentration of talc in the atmosphere was estimated with a Zeiss konimeter in different areas. Samples were taken from an area in the vicinity of the mills, from the stores, from the transport area, from the vicinity of the grinder. The results are shown in Table 3.

About 18 samples of air were taken from Eviex and 14 from Alav. In eight samples of air from the vicinity of the mills and from the transportation area at Eviex it was impossible to make a count because the concentration of talc in the atmosphere was too high and innumerable particles were found on the plaque of the Zeiss konimeter. In the other 10 samples the number of talc particles per litre of air was between 410,000 and 2,150,000.

In two samples from the area near the mills at Alav the talc particles were also too many to count. In the other 12 samples the talc particles per litre of air were between 730,000 and 1,925,000 (Table 3).

TABLE 3
RESULTS OF AIR SAMPLING AT EVIEX AND ALAV

Sampling Sites	No. of Talc Particles per 1,000 ml. Air
Eviex	
Vicinity of the mill (2 samples)	2,050,000 ; 2,150,000
Store area (4 samples)	1,300,000 ; 850,000
..	550,000 ; 410,000
Transportation area (2 samples)	1,350,000 ; 680,000
Vicinity of grinder (2 samples)	580,000 ; 530,000
Vicinity of the mills (7 samples)	Innumerable
Transportation area (1 sample)	Innumerable
Alav	
Vicinity of the mills (5 samples) ..	980,000 ; 940,000
	780,000 ; 795,000
	730,000
Store area (3 samples)	1,925,000 ; 1,730,000
	750,000
Transportation area (4 samples)	1,250,000 ; 915,000
	860,000 ; 810,000
Vicinity of the mills (2 samples) ..	Innumerable

Chemical and Physical Analysis of Talc Samples

We performed chemical analyses of samples of talc made in the factories Similar samples were sent to Professor Paul Bonnevie (Copenhagen) for analyses and estimation of the diameter of the talc particles, and his findings by a refractographic method are as follows (Our own chemical quantitative analyses gave almost similar results. Both these analyses showed no free silicic acid in the samples.) :—

Sample 1 (Eviex, raw material from Hymetos) 51·4% of silicate salts estimated as silicic acid
Sample 2 (Eviex, raw material from Hymetos) 48·0% of silicate salts estimated as silicic acid
Sample 3 (Alav, raw material from Tinos) 49·4% of silicate salts estimated as silicic acid
Sample 4 (Alav, raw material from Tinos) 48·0% of silicate salts estimated as silicic acid
Sample 5 (Eviex, raw material from Hymetos) 51·3% of silicate salts estimated as silicic acid
Sample 6 (Eviex, raw material from Hymetos) 52·2% of silicate salts estimated as silicic acid

Van Wijk and Patterson (1940) and Sayers and Jones (1938) have found that talc particles with a diameter between 5 μ and 0·2 μ are harmful to the pulmonary parenchyma. Estimation of the diameter of the talc particles in the samples by Professor Bonnevie by the Andreasean method gave the following results. Forty-five per cent. of sample No. 1, 87% of sample No. 2, 43% of sample No. 3, 58% of sample No. 4, 92% of sample No. 5, and 98% of sample No. 6 were composed of talc particles with a diameter of 5 μ or less. A high proportion of the talc particles in our samples are therefore capable of producing injury to the lung parenchyma.

Studies of Pulmonary Function

The studies of pulmonary function consisted of spirographic examination, chemical analyses of blood, and the determination of the carbon dioxide and oxygen content of the alveolar and the expired air.

The estimations were made with a Benedict spirograph, a Van Slyke's manometric apparatus for blood gas analysis, and the Orsat apparatus for air analysis, and were carried out according to recognized methods (Van Slyke and Neill, 1924). Some of the estimations were carried out both at rest and after exercise. The exercise consisted of stepping up and down 30 times in one minute on to a stool 20 cm. high.

The formula (Cournand and others (1947) used for calculating the predicted values was maximum breathing capacity (l./min.) = 186·5 – (0·522 × age in years) × body surface area (sq. m.). The patient's surface area was determined from his weight and height by the Du Bois nomogram.

Analysis of Findings

As is shown in Table 2 the values for the arterial blood oxygen at rest in Cases 2 and 7 were substantially lower than normal values, and for arterial blood oxygen saturation at rest in Cases 1, 2, and 7 substantially lower than normal. In all the cases the values of the arterial blood oxygen content and the arterial blood oxygen saturation after exercise were found to be much lower than normal. There was a

definite correlation between these values and the extent of the radiological appearances.

In all cases the transfer gradients were found to be higher than the normal values. Those cases with the more extensive disease had higher transfer gradients. This may be attributed to the inequality of the distribution of oxygen throughout the pulmonary parenchyma owing to the unequal alveolar aeration and the unequal diffusion of air.

As is shown in Table 2 the oxygen consumption decreased with the increase in the extent of pulmonary disease. This may be due to the decreased volume of the air per minute being utilized owing to the destruction of the pulmonary parenchyma and inadequate hyperventilation. The ventilation per minute per square metre of body surface was found to decrease correspondingly with the increase in the extent of disease shown radiologically. The decrease might have been due to insufficient compensatory hyperventilation.

In all our cases the vital capacity was found to be decreased by 19% to 64% of the predicted values (Table 2). The maximum breathing capacity (M.B.C.) was found to be decreased by 18% to 71% of the predicted values. The greater the extent of pulmonary disease the greater was the variation from the predicted values. In six of our cases the ventilation per minute per square metre of body surface at rest was found to be increased above the normal values (Table 2). We are of the opinion that this increase is a compensatory mechanism to combat the destruction of pulmonary tissue.

Discussion

Our cases developed talcosis after a short exposure to talc. Exposure in Cases 1, 2, 4, 5, 6, and 8 varied from 16 to 24 months, and in Cases 3 and 7 from 40 to 60 months. Clinical signs of pneumoconiosis were produced within these periods, and radiological signs, such as scattered mottling of the lungs, in some cases becoming confluent, and "tumour-like" appearances, which were demonstrated in three of our cases, were evident within short periods of exposure. The " tumour-like " appearances are indicative of advanced stages of talcosis. The extent of the disease shown radiologically varied with the time of exposure to the talc-polluted atmosphere and also with the extent of the pollution. Cases 1, 2, 3, and 5 had extensive disease, and worked in a heavily polluted atmosphere for varying times. Case 7, who worked as a mechanic for 40 months, was not exposed to such a heavy talc pollution of the atmosphere as the others and his disease as shown radiologically was not so far advanced.

Follow-up, clinically and radiologically, showed rapid progression of the disease. Radiographs taken at intervals revealed in some cases that the disease progressed from nodule type to " tumour-like " type and there was also a rapid clinical deterioration. One of our patients rapidly deteriorated and died with symptoms of severe pulmonary failure (Case 3).

Our observations allow us to state that pneumoconiosis due to talc is a definite disease. Our findings are not in agreement with those of Sorell and others (1943) who, basing their claims on experimental work, state that talc powder cannot produce the pneumoconiotic plaques which are found in silicosis. These workers were never able to produce experimental pulmonary fibrosis due to talc. For this reason they claimed that pulmonary fibrosis cannot be produced by inhalation of talc if the lung tissue is healthy. They, however, suggested that if pulmonary tuberculosis or other disease which disturbs the bronchial excretion is present, then prolonged exposure to talc may produce talcosis.

More recent research has shown that there is such a clinical entity as talcosis. Our observations confirm more recent work (Gardner, 1938 ; Policard, 1940; Parmeggiani, 1948 ; Bruusgaard and Skjelbred-Knudsen, 1949 ; McLaughlin and others, 1949 ; Baader, 1950) and encourage us to accept the fact that talc can produce a fibrotic pneumoconiosis with functional disturbances.

In our cases the radiological appearances of talcosis were similar to those of silicosis. The lung fields in early cases showed mottling and in more advanced cases " tumour-like " appearances such as are commonly found in silicosis. This agrees with the findings of Pruvost (1946) but Nuck and Szcepanski (1939) describe linear shadowing on the *x*-ray appearance such as is found in asbestosis. We attribute the characteristic *x*-ray appearances to the rapid progression of the disease and the appearance of lesions in both the interstitial pulmonary tissue and pulmonary parenchyma. Fletcher, Mann, Davies, Cochrane, Gilson, and Hugh-Jones, (1949) suggested that secondary tuberculosis is responsible for the " tumour-like " *x*-ray appearances. In our cases, some of which had these " tumour-like " appearances, there was no evidence of secondary tuberculosis, but it is known that cases of progressive massive fibrosis in coal miners have repeatedly negative sputa for *M. tuberculosis* in spite of the fact that pathological examination revealed tuberculosis.

We are of the opinion that the " tumour-like " appearances on the radiographs of some of our cases was due not to fibrosis alone but to concretions

of talc obstructing the bronchioles and causing areas of atelectasis, this being responsible for a further secondary fibrosis which results in increasing the fibrotic tissue already present due to irritation of the pulmonary parenchyma by the inhalation of talc.

The rapid development and progression of pneumoconiosis due to talc in our cases must be attributed to the lack of preventive measures taken against the inhalation of the powder, to the high concentration of talc particles in the atmosphere with a diameter of 5 μ or less, and also to the high content of silicates in the talc as shown by analyses. Chemical analyses of our talc samples have shown that there is no free silicic acid in this talc. According to the majority of writers free silicic acid is the causative factor in the production of silicosis.

Our analyses of pulmonary function studies are indicative generally of several degrees of impaired pulmonary function. The results of the analysis of these findings suggest that ventilatory as well as alveolar respiratory insufficiency was present. It is possible that the fibrotic changes found in talcosis produce changes in alveolar aeration and perfusion. It is evident that this is an important factor in the production of pulmonary insufficiency.

Summary

Eight cases of talcosis occurring in mill workers and developing after an unusually short exposure to talc are described.

The radiological appearances and clinical findings in these cases were similar to those found in silicosis.

The chemical analyses of samples of talc powder did not reveal the presence of free silicic acid. It was evident that the gross pollution of the air in the factories and the small diameter of the talc particles were the main contributory factors in the production of talcosis.

Talcosis may be considered a type of fibrotic pneumoconiosis accompanied by functional disturbances.

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INJURY TO THE RESPIRATORY TRACT BY ISOCYANATES USED IN MAKING LACQUERS

BY

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Bayer, Rinke, Siefken, Orthner, and Schild in 1937 and 1942 demonstrated the possibility of producing high molecular compounds with extraordinary chemical and physical properties by means of a so-called diisocyanate-polyaddition procedure. The basic reaction, leading to low-molecular products, had been known for about 100 years. Bayer and his colleagues were able to show, however, that the reaction between a diisocyanate, *e.g.*, 1,6-hexane-diisocyanate and a divalent alcohol, *e.g.*, 1,4-butylene-glycol, led to the formation of a linear polymer, a polyurethane that could be spun. This product was given the name " perlon U". If the reaction takes place between a diisocyanate and compounds with more than two hydroxyl groups, *e.g.*, alkydresins with free OH-groups, one obtains high-molecular compounds with a network structure. Through the variation of the polyester types (the alkydresins) it is possible so to change the properties of the final product that one gets hard and brittle products of alkyds built upon glycerol and phthalic acid as well as soft and elastic products of alkyds built upon aliphatic carbonic acids and glycols. The di- or tri-isocyanates have been given the trade name " desmodur " with varying designations according to particular type, while the polyesters are called " desmophen". Of over 100 diisocyanates, only about 15 can be produced technically. Of interest are the " desmodur " types T, TH, and THN. " Desmodur T " consists of a mixture of 60% m-tolylene diisocyanate and 40% p-tolylene diisocyanate. It is a fluid with low viscosity with a flash point of + 132° C. and melting points of + 5 to + 7° C. At the time of the cases described in this paper probably only " desmodur TH " was used in Sweden. This is a compound of 3 mol. " desmodur T " and 1 mol. hexane triol (Bayer, 1947). It consists of an almost odourless resinous mass which appears commercially dissolved in a solvent such as ethyl acetate or in a mixture of ethyl acetate and toluene. It contains about 15% of the primary substance " desmodur T " (Reinl, 1953). More recently, Farbenfabrik Bayer in Leverkusen has also produced " desmodur THN", whose composition is not known to us. In this product, too, however, one may probably assume that there are traces of " desmodur T". The isocyanates are chemically extraordinarily reactive and combine easily with primary NH_2-groups, water, alcohols, carbonic acids, phenols and, in general, with compounds having a reactive hydrogen atom which may theoretically be replaced with an alkali metal.

Use of Desmophen and Desmodur

The two components " desmophen " and " desmodur " in suitable solvents are mixed in stoicheiometric proportions just before use. After half an hour to an hour the mixture may be applied by means of brushing, dipping, or spraying. The reaction between the components takes place at ordinary temperatures, which makes the lacquer a suitable material for corrosion-resisting and chemically stable protective coatings for metal, wood, and concrete. The electric resistance of the lacquer is high, which renders it useful as an insulating covering.

Physiological Properties

There are in the literature extremely few reports of the toxicity of the compounds mentioned. The final product and the " desmophen " types are considered to be physiologically inactive.

Diisocyanates with relatively high vapour pressures such as " desmodur T " are physiologically highly active, while TH is said to be without vapour pressure and without toxic effect (Bayer 1947 ; Hebermehl, 1948). As far as we have been able to ascertain, however, no study on the toxicity of this compound has been published. With 2,4-tolylene diisocyanate, which forms the main component in " desmodur T ", Gross and Hellrung (1941) have carried out unpublished experiments (Reinl, 1953) with mice, rabbits, and cats. When it was administered subcutaneously to mice the animals tolerated more than 10 g./kg. body weight without reaction. According to information we have received from Du Pont Rubber Laboratory, U.S.A., tests of 2,4-tolylene diisocyanate (TDI), which corresponds to " desmodur T ", have shown the minimum lethal dose of this substance for white mice to be 4·8 to 6·0 g./kg. body weight. A certain cumulative effect has also been demonstrated (Neal, 1953). Fuchs and Valade (1951) state that on subcutaneous administration of an oil-solution of " desmodur T ", guinea-pigs tolerate more than 500 mg./kg. body weight without reaction.

Gross and Hellrung (according to Reinl, 1953) found that undiluted " desmodur T ", applied direct to the ears of rabbits, could cause reddening, swelling, and necrosis, which healed with formation of a crust. The degree of the injury depended upon the duration of the exposure. One drop of " desmodur T " in the conjunctival sacs of rabbits resulted in an immediate lacrimal flow and pronounced irritation, a marked inflammatory reaction.

Gross and Hellrung also carried out inhalation experiments with four-hour exposures of rabbits and cats. The concentrations used are not given. The animals reacted with pronounced irritation of the mucous membranes of the eye and nose. Higher concentrations resulted in irritation further down in the respiratory passages. A number of animals died after the experiment, and necropsy showed oedema of the lungs, pneumonia, bronchitis, and tracheitis. In one or two cases the kidney was damaged.

Fuchs and Valade (1951) performed inhalation experiments with monkeys, rabbits, and guinea-pigs. The inhaled air contained 1 to 2 g. " desmodur T"/m^3. The rabbits and guinea-pigs reacted with sneezing, polypnea, and lacrimation. All the symptoms rapidly disappeared when the exposure was discontinued and all the animals survived.

Effects of Industrial Exposure

There are very few published data of injuries after industrial exposure to these substances. The first publication we have been able to find is an article by Fuchs and Valade (1951), who examined the workers in a factory for the production of a plastic mass with vinyl resins and " desmodur T " as primary materials. They state that during a first period, varying between eight days and two months, the workers had no serious trouble but merely complained of a slight irritation of the mucous membrane of the conjunctiva, slight lacrimation, and prickling sensations in the throat. After this appears progressive bronchial irritation with an irritating dry cough and dyspnoea, which may be at its worst during the night and prevent sleep. Asthmatic attacks may also occur. The symptoms recede quite rapidly when the exposure is discontinued, only to return in many cases in the form of an acute attack on renewed, even very short and slight, exposure.

Holmquist, Lundgren, and Swensson (1953) made the same observations as Fuchs and Valade. The findings were further confirmed by Reinl (1953).

At the Department of Occupational Medicine we have so far had occasion to examine and follow up 15 patients with more or less severe symptoms from the respiratory passages as a result of exposure to " desmodur ". In all these cases the symptoms manifested receded in a short time after cessation of exposure. The picture and course of the affection are fairly monotonous, and the different cases show only minor variations, so we give only illustrative, typical cases.

Case Histories

Case 1.—B. G. T. N.-n., born in 1912, did not as a rule easily catch cold. He had never had any pulmonary affection or asthma nor had he any family history of allergy.

About three months before examination he began spray-painting with polyisocyanate lacquer. He worked in a room with a ventilated spray-painting booth, but this was not sufficient to control the vapours from spraying. After two months he began to have trouble from the respiratory tract, with an irritating cough and dyspnoea but no sputum. He was better during the holidays. He returned to work again for one week and had increasing shortness of breath, pressure on the chest, and coughing without sputum. He then attended the out-patient department on July 29, 1953.

On examination it was found that he had no dyspnoea when resting but slight dyspnoea when walking, inconsiderable pharyngitis, a normal heart, and a blood pressure of 145/100 mm. Hg. Rhonchi and rales were heard all over the chest.

The sedimentation rate was 3 mm., Hb 92%, white blood corpuscles 4,100 per c.mm.

A radiograph of the lungs on July 29 showed no

parenchymal or pleural shadows and the hilar shadows were normal.

Spirometry on August 6 gave a total capacity of 7·94 litres, a vital capacity of 6·67 litres, and a residual quotient of 18%. These are normal spirometric values.

Separate skin tests with the different constituents of the lacquer were negative.

In this case we have the picture of asthmatic bronchitis in a man who never previously had any asthmatic trouble or more pronounced symptoms of any kind from the respiratory tract. We have no evidence that an infection of the upper respiratory tract played any role. He showed impaired lung function of the kind met with in asthma, which recedes when exposure is discontinued. What remains for a longer period is a subjectively increased sensitivity to the odour of solvents.

Case 2.—B. S. D.-t. was born in 1914 and had no family history of allergic affections or of asthma. Hitherto he had always been healthy, and had had no respiratory ailments.

In 1951 the patient studied polyisocyanate plastic painting in Germany where he worked in an old cellar. During the first period he had only slight symptoms of irritation from the respiratory tract. He then caught cold and had severe bronchial symptoms with pronounced dyspnoea, whistling in the chest when breathing, and fits of coughing but no expectoration. He has since been sensitive to "desmodur" and has reacted with asthmatic symptoms at every exposure, perhaps a couple of hundred times. He is now extremely sensitive and even had a reaction from being in the same room as another person who had been present for a time while plastic spray-painting was going on. He is able to state, moreover, that it is the "desmodur" component he is sensitive to for he comes into contact with other solvents without any symptoms being caused.

Each separate attack recedes, as a rule, after 10 to 12 hours, and he then feels fit again. He has never had similar attacks from any other cause.

He attended the out-patient department on May 29, 1953.

On examination he had dyspnoea when resting, noticeably increased during conversation or while walking. The throat was normal. Expiration was prolonged, and rhonchi were heard diffusely over both lungs. The heart was normal. Blood pressure was 150/90 mm. Hg.

The sedimentation rate was 3 mm., Hb 100%, white blood corpuscles 6,700 (5·5% eosinophils).

Spirometry gave a total capacity of 7·11 litres, a vital capacity of 3·59 litres, and a residual quotient of 50%. Spirometric values were as in pronounced emphysema, namely a large total capacity, small vital capacity and complementary air, and a large residual capacity in relation to the total capacity. He was given 10 µg. adrenalin intravenously which resulted in immediate but transient subjective relief. In response to theophyllamine glucose the symptoms rapidly disappeared, and the patient has since been free of symptoms.

In this case the asthmatic reaction seems to have appeared for the first time concurrently with an infection of the upper respiratory passages, and after this the hypersensitivity has become permanent so that the patient has reacted with asthmatic attacks on renewed exposure.

The possible importance of an infection for the appearance of the symptoms must also be considered in the following case.

Case 3.—E. O. W.-m., born in 1914, was repeatedly treated for an ulcer and had an obstinate cold in the spring of 1953.

A radiograph of the nasal sinuses on February 2, 1953, showed swelling of the basal mucous membrane in the large left frontal sinus while the right sinus appeared on the whole normal. Shadows were seen in the ethmoidal cells of both sides, pronounced swelling of the mucous membrane in both maxillary sinuses, and swelling of the left nasal cavity. The *x*-ray picture was otherwise normal. The patient had no family history of asthma or other allergic complaints. He has been a painter since leaving school.

Since the middle of March he had been engaged in spray-painting with plastic lacquer, with a short period of brush-painting. He stated that when spraying he wore an air-line respirator but for certain jobs was unable to wear a mask. After the first day's spraying he had a severe cough in the night so that he had to sit up in bed for an hour. On succeeding days he felt pressure on the chest while working, and thought he was not getting any air. He had to go out in the fresh air every now and then to breathe and felt relief on these occasions. He had a rather severe irritating cough but no sputum. The cough was especially trying at night. He found it difficult to remain lying down and often had to sit up for three or four hours on account of cough. He stopped work after two weeks' spray-painting and symptoms have since then slowly receded. He still feels tired. The cough now appears chiefly on physical effort, but dyspnoea is not troublesome.

He attended the out-patient department on April 23, 1953.

On examination he appeared healthy with no dyspnoea, a normal pharynx and heart. The blood pressure was 150/70 mm. Hg and the lungs were normal.

The sedimentation rate was 5 mm., Hb 93%, white blood count 7,000 (differential count normal, eosinophils 2%). A radiograph of the lungs was normal.

A radiograph of the nasal sinuses showed as before a slight swelling of the mucous membrane in the left frontal sinus. The ethmoidal cell regions on both sides were rather denser than before and the shadow in the maxillary sinuses had somewhat increased. No levels were visible. A test puncture of the maxillary sinus bilaterally yielded nothing.

Spirometry gave a total capacity of 8·36 litres, a vital capacity of 5·50 litres, residual quotient 34%, and indicated slight emphysema.

Nothing pathological was seen on an E.C.G. at rest and an ordinary reaction was obtained after work.

A feature common to all the cases is a family and personal history without asthma and bronchial symptoms, and that the current symptoms had first appeared after exposure for a shorter or longer period without severe symptoms. In some cases an infection of the upper respiratory passages has acted as a trigger, but this is by no means always the case. On discontinuance of the exposure the symptoms gradually recede, but increased sensitivity appears to remain so that on renewed exposure the symptoms return at once.

Prophylaxis

Owing to the irritating effect of " desmodur T " upon the mucous membrane it is important to take adequate precautions. This is the more necessary in view of the sensitizing capacity of the substance.

In spray-painting in a spray-booth the face-velocity of the air commonly used with ordinary paints should probably be considerably increased. Preferably, an air-line respirator should be used. In brush-painting out of doors there is probably sufficient ventilation, but in indoor work respiratory protection is desirable, at least in bigger jobs and on prolonged work.

In connexion with the cases of poisoning described we did not carry out any air analyses to determine the content of " desmodur " in the atmosphere. It is, however, a fairly simple matter to determine the number of reactive NCO-groups by coupling to a secondary amine in a suitable solvent, *e.g.*, chlorobenzene. Unconverted amine may thereafter be back-titrated with hydrochloric acid (Bayer, 1947). The value of air analyses appears to us to be limited in view of the sensitizing capacity of the isocyanates.

It is important that all who work with " desmodur " compounds should be informed of the risks entailed in the work and how protection may be achieved.

Therapy

The irritation in the conjunctivae and respiratory passages is slight and disappears rapidly. As a rule, no treatment is required ; only in exceptional cases may symptomatic treatment be in order. The rational treatment is to reduce the exposure with adequate technical measures. This will also reduce the risk of sensitizing those exposed. The asthmatic attack, when sensitization has occurred, calls for ordinary symptomatic treatment. When the acute reaction has subsided the patient should be protected from renewed exposure.

Summary

A number of isocyanates which are used for the production of certain lacquers may cause symptoms of irritation from the mucous membranes of the eye and the respiratory passages. In addition to this, sensitization may occur whereby renewed exposure will give rise to regular asthmatic attacks.

Previous investigations are reviewed and typical cases are described. Technical protective measures are discussed.

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DIMETHYL SULPHATE POISONING

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Dimethyl sulphate ($(CH_3)_2SO_4$) has been used since the beginning of the century as a methylating agent in the preparation of organic chemical products and colouring agents, in the perfume industry, and in other processes. It is a colourless or yellowish liquid of oily consistency which vaporizes at 50° C. and has a slight piquant smell. Both the liquid and the vapour are vesicants and by virtue of this property may be used in warfare.

Following exposure there is an intense local action on the skin and mucous membranes. The skin changes vary from a simple redness to vesication according to the length of contact. Genital and mucous membrane lesions, which are due to the vapour only in most cases, may be delayed for some hours. Changes in the eyes consist of conjunctivitis, oedema of the lids, photophobia, lacrimation, and, in severe cases, keratitis. In the upper respiratory tract oedema or even ulceration of the lips and pharynx are prominent features, together with involvement of the nose, larynx, and trachea. There can also be systemic effects, such as convulsions, coma, analgesia, pyrexia, leucocytosis, albuminuria, and pulmonary oedema.

It is uncertain whether the lesions are produced by the action of the whole molecule of dimethyl sulphate or by the products of its hydrolysis, sulphuric acid and methyl alcohol.

In spite of the widespread use of dimethyl sulphate in industry, cases of poisoning are seldom seen. The following cases are reported for this reason and because they showed certain features not previously recorded.

Case Reports

Case 1.—A. H., aged 20, a male chemistry student, while working in a laboratory on October 28, 1953, dropped and broke in a fume cupboard a 2½-litre bottle almost full of dimethyl sulphate and the liquid poured over the edge soaking through his trousers to involve the genitalia and left thigh. His hands were completely covered by the liquid. He immediately washed his hands and treated his trousers with water and 5% N. caustic soda and sodium bicarbonate. Fifteen minutes later he removed the trousers and was washed down with strong ammonia, the trousers receiving similar treatment. There was no tingling or burning sensation in the affected areas though the skin was a little reddened. About one hour after the accident he put on his trousers again and went to a casualty department where a sodium bicarbonate paste was applied to his thighs. He was then feeling perfectly well and, two hours after the accident, attended a lecture. During this he noticed a smell of dimethyl sulphate and a slight soreness of the genitalia.

Three hours after the accident the genitalia were swollen and pink, his eyes were bloodshot, and later his vision became blurred. Four hours after the accident his eyes had become painful, he could not open them, and he was admitted to a hospital casualty ward. He then started to feel ill and was transferred to an eye hospital. Here gross oedema of the lids and extensive excoriation of the corneal epithelium of both eyes was seen. Local treatment with atropine 1% and liquid paraffin was started but owing to the appearance of severe upper respiratory symptoms he was transferred to this hospital eight hours after the accident.

On admission he was obviously distressed, and was complaining of painful eyes, difficulty in breathing, and retrosternal pain. On examination his pulse rate was 116/min. and his temperature rose to 99·2° F., oedema of the eyelids was extreme and the corneae excoriated. His nose was running, the uvula was swollen, his voice was hoarse and there was marked bronchospasm. Moist sounds could be heard all over the chest.

Treatment was started with atropine, morphine, penicillin, and steam inhalations, and he was placed in an oxygen tent. Thirteen hours after the accident large blisters were noticed on the penis and there were smaller blisters on the scrotum and left thigh. These were covered with sodium bicarbonate compresses.

During his first night in hospital (16 hours after the accident) he coughed up a piece of tissue about 2 in. by 1 in. This was examined microscopically and appeared to be necrotic tracheal mucosa (Fig. 1). The next morning surgical emphysema was felt in the left subclavicular area and it subsequently spread to involve the neck and face (Fig. 2). The patient was able to take fluids by mouth without much distress and it was therefore

FIG. 1.—Tracheal mucosa expectorated by Case 1. It has been divided into four pieces during pathological examination. (Scale in cm.)

considered that the surgical emphysema was coming from a perforation of the trachea.

On October 29 he was still very ill and distressed by an irritating cough. A blood count revealed a leucocytosis of 25,000 per c.mm. with 90% polymorphonuclear leucocytes; the haemoglobin was 120% (Sahli) and the red blood corpuscles numbered 6,090,000 per c.mm. The urine contained a moderate amount of albumin and a few red blood cells.

On October 30 the eye symptoms had lessened and there was no obvious corneal opacity. The bronchospasm had gone but he still had retrosternal pain and was expectorating mucopurulent sputum. The moist sounds had disappeared and the oxygen tent was therefore removed. A radiograph showed normal lung fields and demonstrated the surgical emphysema, which had increased. Serum was pouring from the burnt areas of the penis and scrotum. The oedema of the uvula had subsided and his swallowing was easier.

The condition of his eyes and upper respiratory tract improved steadily during the next week and penicillin

FIG. 2.—Surgical emphysema of neck and face.

was then discontinued. On November 6 his eyes showed only slight injection, but there was still photophobia. His voice was still husky but his breathing and cough were much improved, and the surgical emphysema was disappearing. The pyrexia had settled, the albuminuria had disappeared, haemoglobin was 90%, and white blood cells were 10,000 per c.mm. with 84% polymorphonuclear leucocytes. However, the penile and scrotal burns had become infected; large sloughs eventually separated from the scrotum and the prepuce.

On November 8 there was a recurrence of bronchitis with pyrexia and a course of aureomycin was started. By November 16 he was completely recovered except for the granulating areas on the genitalia, and he was discharged three weeks later.

When seen as an out-patient on January 25, 1954, he appeared well but complained of his eyes aching after reading for a short time. An ophthalmologist could find no abnormality and considered that there was a psychological factor. Laryngoscopy revealed a crescentic scar on the anterior wall of the trachea about $\frac{3}{4}$ in. below the vocal cords, extending about one-third round it but causing no appreciable narrowing of the lumen. This was probably the site of origin of the tissue which he coughed up within 24 hours of the accident.

The genital burns had healed, leaving a stricture of the prepuce which could not be retracted. A circumcision for this was performed on March 31.

Case 2.—D. M., aged 28, was a male process worker employed by a small chemical firm. In November, 1951, he was engaged in the manufacture of an analgesic drug, and in the process dimethyl sulphate was gradually added, as a methylating agent, to a mixture of phenazone and sulphuric acid in a 20-gallon refrigerating pot. This methylating plant was in the open air near the door of the building in which the rest of the process was carried out. On November 21 the patient emptied the refrigerating pot but otherwise did not work with dimethyl sulphate. On November 22 he arrived at work at 8 a.m., changed into the working clothes he had worn the previous day, and then walked past the methylating plant into the building and worked on a process in which dimethyl sulphate was not used. At 10 a.m. he noticed that he had lost the upper half of his visual fields. He was told to breathe ammonia and found he could not smell it. By 11 a.m his upper lids were drooping so much that he could hardly see and he was then taken to an eye hospital. When he arrived there he could not see at all but had no symptoms of discomfort. Five hours later he felt that his penis was swollen though it was not sore, and during the evening his breathing gradually became difficult and he was transferred to the Liverpool Royal Infirmary.

Twelve hours after his first symptoms he had gross swelling of the eyelids, chemosis, excoriation of the corneae, and marked oedema of the soft palate and uvula; there was bronchospasm, and moist sounds could be heard in all parts of the chest; the penis and scrotum were swollen and vesicated. On admission his temperature was normal and it remained so for 24 hours; it then rose to 99–100° F. for two days and was normal

thereafter. The pulse rate was 50 per minute on admission and during the first 24 hours in hospital it did not rise above 65 per minute; his normal pulse rate was found to be 75 to 85 per minute after recovery.

Treatment was started with atropine, sulphacetamide, and liquid paraffin drops to the eyes, penicillin intramuscularly, and he was placed in an oxygen tent. By next morning his breathing was easier though the rate was 25 to 30 per minute. The oedema of the fauces slowly subsided and the moist sounds gradually disappeared from the chest. He had to be catheterized for two days after admission. The burns of the penis and scrotum became infected and sloughs later separated.

The eye condition improved gradually and by December 13 only a traumatic conjunctivitis remained, the corneae being clear. However, he still complained of photophobia and this symptom persisted until April, 1952.

He was discharged from hospital on January 4, 1952, the question of circumcision having been raised as the prepuce had become tight and had to be forced over the glans penis. No operation was performed and recovery was complete with no residual diability.

Discussion

Both cases showed the typical symptoms and signs of poisoning by dimethyl sulphate vapour. How Case 2 became contaminated is uncertain but it is possible that his working clothes were splashed at the end of one day's work and he got burnt after putting them on again next day.

Though both cases were typical, they showed the different modes of presentation which are possible. One man was very distressed with painful eyes and retrosternal pain, whilst the other, almost as badly burnt, had no discomfort for nearly 24 hours. This analgesia has been described in experimental animals by Auer (1918) who found that it may last for as long as six months; he also states that soldiers in the field can undergo surgical procedures without anaesthesia if they have been gassed by dimethyl sulphate (Auer, 1922). It is interesting that Case 2 required no analgesics for one week after admission.

The tachycardia in Case 1 was found in two cases reported by Mohlau (1920). We have not found any reference in the literature to the bradycardia which was a prominent feature in Case 2 during the first 48 hours.

The haemoconcentration and albuminuria which were found in Case 1 48 hours after admission have been previously described (International Labour Office, 1930). Peripheral neuritis such as described by Cuthy (1940) was not present in either of our cases.

Another feature not previously described in the literature is the surgical emphysema which developed in Case 1. It was presumably due to air leaking through the weakened tracheal wall at the site from which he had lost the mucosa; probably air only escaped into the tissues during bouts of coughing.

The prognosis in dimethyl sulphate poisoning has been improved during the past 10 years by the use of antibiotics in the control of respiratory tract infections.

In several reports of cases of dimethyl sulphate poisoning (Mohlau, 1920; Bodenstein, 1921; Strothmann, 1929; Merkelbach, 1943; von Nida, 1947) we have been unable to find any reference to the use of oxygen in treatment. We believe that the oxygen tent and steam inhalations are most valuable in relieving respiratory distress.

If patients do not die from dimethyl sulphate poisoning, recovery is usually complete, but some symptoms and disability may persist for months. Photophobia, colour blindness, and some loss of visual acuity were reported by Mohlau (1920) to be still present six weeks after poisoning. In Case 1 some aching of the eyes when reading was present three months after admission and in Case 2 the photophobia persisted for four to five months. Extensive scarring of the prepuce may necessitate circumcision, as happened in one of our cases.

Summary

The physical properties of dimethyl sulphate and its uses are briefly described.

Two cases of poisoning showing the typical clinical picture are reported.

Bradycardia and surgical emphysema affecting the face and upper thorax were features not previously recorded.

The value of antibiotics and oxygen in treatment is stressed.

We wish to thank Dr. E. Wyn Jones for permission to publish Case 2 which was under his care. Our thanks are also due to Dr. H. S. Pemberton, Dr. A. Thelwall Jones, and Dr. A. Lloyd Potter for their advice and help in the preparation of this paper.

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VANADIUM POISONING FROM GAS TURBINES

BY

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Vanadium pentoxide poisoning has been described in men working in plants processing vanadium ore by Symanski (1939) and Sjöberg (1950), and twice (Wyers, 1946 ; Williams, 1952) in men exposed to the soot of fuel oil burned in boilers. It does not, however, appear to have been described before in men who work on gas turbines. Since these may become much more common in the future as sources of power using residual fuel oil for generating stations, ships, and locomotives, and also possibly for cars and omnibuses, it is worth bringing together the medical, engineering, and preventive aspects of the problem as far as they are known at present.

Vanadium is found in all fuel oil and remains in the residual heavy oil after the more volatile fractions, such as petrol, paraffin, and diesel oil, have been distilled. It is, therefore, only a constituent of the exhausts of gas turbines using heavy residual fuels. Vanadium, which is present in the natural oil in complex compounds, appears as the pentoxide after combustion, and this forms an acid solution in water.

To improve the thermal efficiency of some types of gas turbine, the exhaust gas is made to heat the air from the compressor, and this is done in a heat exchanger which may take the form of a large metal box filled with tubes, outside which the hot exhaust gas flows. The intake air is inside the tubes which are arranged in a particular configuration. The products of combustion are deposited on the outside of these tubes. But in some types of heat exchanger the relative situations of exhaust gas and intake air are reversed, and in these the products of combustion will be deposited on the inside of the tubes. The 12

TABLE
ANALYSIS OF SYMPTOMS

Patient No.	Respiratory System						Alimentary System					Skin			Other	Total	Days before Symptoms
	Nose		Chest				Black										
	Blocked	Bleeding	Cough	Breathless	Wheezing	Tightness and Pain	Tongue	Teeth	Odd Taste	Nausea	Diarrhoea	Sore	Smarting Eyes	Rash			
1	+				+	+							+			4	1
2			+				+					+				3	4
3			+												+	2	Not known
4	+	+				+	+			+	+			+		7	14
5		+	+				+	+	+							5	3
6	+	+	+	+	+											5	2
7		+														1	3
8							+		+							2	7
9			+			+	+									3	2
10		+				+	+	+	+			+				6	7
11			+	+	+				+			+				5	2
12	+				+	+							+			4	1
Total	4	5	6	2	4	5	6	2	4	1	1	3	2	1	1	Average : 4·2	

affected men in the present description were working inside a heat exchanger cutting away the tubes with pneumatic chisels. The exhaust air from these made a dust, and after an average time of just over four days in these conditions the men complained of the symptoms shown in the Table on page 57.

Two out of 12 of the men noticed symptoms in one day, three in two days, two in three days, one in four days, two in seven days, and one man was only affected after 14 days' exposure. Nose bleeding was the first symptom in five men and, in general, the acute respiratory symptoms of cough, tightness or pain in the chest, wheezing or breathlessness, predominated, followed by alimentary and skin effects. Eight of the men complained that their tongues or teeth had become black, and four of having an odd taste in the mouth. A few said they had a sore skin or smarting eyes, but only one man complained of a rash. After exposure to the vanadium pentoxide was stopped the symptoms of black tongue or teeth ceased in from two to four days, but the respiratory symptoms took from seven to 14 days to disappear. The symptoms in the present series of cases are generally similar to those described by Williams (1952), except that there was bleeding rather than running of the nose. Skin effects were not noticed in his series, nor mental depression in this series.

Chemical Engineering

The deposit on the outside of the heat exchanger tubes which the men were cutting away was heterogeneous, and consisted of three layers of different composition which related to the different fuels which had been used (Fig. 1). The outer of these three layers formed dust much the most easily, so that the dust to which the men were exposed probably contained at the least 11% of vanadium, and at the most 20%. These figures are rather higher than those found (6·1 to 12·7%) in the soot of the oil-fired boilers described by Williams. But the ash analysis of a normal residual fuel supplied by the Petroleum Board may contain as much as 62% of vanadium pentoxide (Hughes and Voysey, 1949).

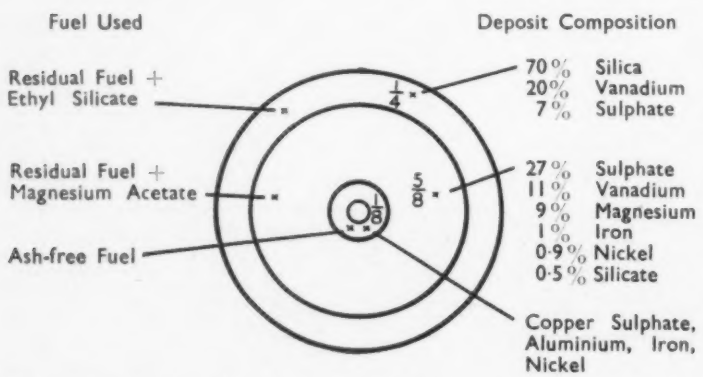

FIG. 1—Diagram of the three fuels used and the relative thickness and composition of the deposits which they formed round the heat exchanger tubes.

Prevention

The prevention of this type of industrial vanadium poisoning is complicated by the fact that the dust produced forms an acid solution in water which irritates the skin. The working area in the present study was wet, and complete protection was afforded the men by dressing them in waterproof clothing, gum boots, and a civilian duty gas mask with an external air supply. There were no further symptoms after the prescription of this protective clothing, although the work continued as before.

Heat exchangers will probably be used in conjunction with gas turbines wherever efficiency is considered important, as in marine installations. But it may be that the tubes can be cleaned, other than manually, by blowing a jet of air or steam over them at a stage before they have developed much deposit. If they are found to scale up further after considerable use it may be possible to cleanse them chemically, and it is only if these two methods fail that men will need to work inside the exchanger. Further engineering experiments will be needed before it can be said which method or combination of methods works the best.

Public Health Aspects

All residual oils have a certain amount of vanadium in them, and the proportion appears to be higher in fuel from Venezuela. Gas turbines to use fuel of this type are at present being developed for ships, power stations, and locomotives, and it may well be that in the future diesel engines will also start using this fuel, because it is cheaper than the diesel oil at present used which is a distillate and contains no vanadium. In all these cases the exhaust, which may contain a vanadium respiratory irritant, will be discharged into the air.

Vanadium pentoxide, V_2O_5, is as great a nuisance to the engineer as it is to the doctor, since it corrodes the blades of gas turbines. Two methods are used to overcome this: either to introduce a metallic oxide or acetate with which the vanadium pentoxide

unites to form an inactive vanadate, or to introduce a silicate so that vanadium silicate is formed which passes through the turbine as a fine dust. In the present experiments both these methods were used at different times, but the resulting deposits, presumably either vanadates or silicates, were still powerful irritants to the human respiratory tract, as shown by the symptoms of the men who inhaled them. The concentration of these compounds in the gas turbine exhaust is 20 to 60 p.p.m. (by weight), depending upon the temperature conditions under which the turbine runs. In the present experiments the inlet temperature to the turbine was 650° C. It is not known what the concentration will be in the exhausts of diesel engines using residual fuel, but it may be higher due to the lesser quantity of excess air used.

In the future vanadium may take its place alongside sulphur dioxide and the carcinogens as part of the smog problem, but at present we do not know either what concentrations are likely in areas round power stations, or in their stack gases, or in a street of stationary diesel buses. Neither can we yet state the maximum permitted concentration in the atmosphere. Symanski (1939) showed that young men of good physique developed chronic bronchitis from working for a few years in a vanadium factory, and the work of Wyers (1946) strongly suggests that continued inhalation of these compounds causes chronic bronchitis and emphysema—and under his conditions quite rapidly. This suggestion is supported by the work of Sjöberg (1950), who demonstrated that rabbits which were exposed to 0·02 to 0·04 mg. per litre of vanadium pentoxide dust for one hour a day for eight months developed emphysema which could be seen post mortem.

Summary

Twelve cases of vanadium poisoning are described in men working in a gas turbine heat exchanger. The symptoms were acute irritation of the respiratory tract, with nose bleeding and blackening of the tongue and teeth. Irritation of the skin and eyes was also reported.

The vanadium was in the form of a silicate, vanadate or pentoxide, and formed 11 to 20% of the deposit on some tubes which the men were cutting away.

The immediate prevention of the condition is by means of waterproof protective clothing and breathing through a mask with an external air supply. Applied chemical engineering may make this job unnecessary in the future.

Gas turbines and diesel engines which use residual oil as a fuel will contain vanadium compounds in their exhausts to the atmosphere. This may provide a public health problem, but little is yet known about the concentrations concerned.

Acknowledgments are due to T. W. F. Brown, D.Sc., Director of the Parsons and Marine Engineering Turbine Research and Development Association, Wallsend, Northumberland, and his staff for help over the chemical engineering of this problem.

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THE TOXICITY OF OZONE IN THE PRESENCE OF OXIDES OF NITROGEN

BY

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In a previous paper we (Diggle and Gage, 1954) have referred to published statements that the toxicity of ozone is increased if oxides of nitrogen are present and we have suggested the hypothesis that if, in fact, this is so, then the increased toxicity is likely to be due to the presence of nitrogen pentoxide, to which the lower oxides of nitrogen are converted by ozone. As a first step to establish this, we undertook a study of the toxicity of nitrogen pentoxide and we demonstrated that it is a " lung irritant " gas of high potency.

Since the appearance of our paper, a careful review of the literature on the toxicity of ozone has been made by Stokinger (1954) from which it is evident that although there is general agreement that ozone produces pulmonary oedema and emphysema, there are wide variations in the concentrations which are regarded as necessary to produce these symptoms. A direct comparison of the results of various investigators is rendered difficult by the use of different experimental conditions and species, by different degrees of purity of the ozone, and by deficient or faulty analytical control of the test atmospheres.

In the investigation described in the present paper, we have measured the toxicity of ozone to rats and the effect thereon of the presence of added amounts of nitrogen dioxide, and we have studied the extent to which this can be attributed to the analytically determined amounts of nitrogen pentoxide present. We have also made analytical measurements on an industrial atmosphere where conditions are favourable for the production of ozone together with oxides of nitrogen.

Preparation of Test Atmospheres

Ozone generated by means of a silent discharge ozonizer (Tack Air Conditioning Ltd., Model LO3). Oxygen (99·5%) was passed from a cylinder through the ozonizer at a rate of 1 to 3 l./min. ; at this rate the ozone output was of the order of 27 mg./min. The ozonized oxygen was allowed to leak at controlled rates in the region of 20 ml./min. into a stream of filtered air which had been dried by means of a silica gel column to a humidity of about 10%. Analytical control of the ozone dilution demonstrated that provided the flow rates were maintained constant, the ozone concentration of the atmosphere produced remained constant for the duration of each experiment. The ozone dilution passed through a 5-l. mixing vessel and thence to the exposure chamber. The exposure chamber was constructed, as described in our previous paper, from a 20-l. glass desiccator ; the inlet and outlet tubes were sealed into the chamber by means of polythene bungs and all flexible connexions in the system were made with polyvinyl chloride tubing.

The nitrogen dioxide-ozone mixtures were prepared by adding nitrogen dioxide to the air used to dilute the ozonized oxygen. Pure nitrogen dioxide, prepared as previously described, was passed into a flask cooled to −80° C. in a solid carbon dioxide-acetone freezing mixture. A proportion of the air stream, according to the concentration required, was diverted through this flask, entering it by a jet situated within 1 cm. of the surface of the solid nitrogen dioxide maintained at −80° C. Analytical control demonstrated that the atmospheric concentrations so produced were reasonably constant.

Analytical Methods

Ozone.—After a critical review of methods of determining ozone in air, Wilska (1951) has selected the iodometric method of Gluckauf, Heal, Martin, and Paneth (1944) who recommended absorbing the gas in a potassium iodide solution buffered to *p*H 7. This procedure has been followed in the present investigation ; air was sampled at intervals from the outlet of the exposure chamber at 4 l./min. through an absorber (Gage, 1952) containing 10 ml. buffered potassium iodide solution. The contents of the absorber were washed into a titration flask with 25 ml. water and titrated with 0·01 N sodium thiosulphate. By means of control experiments with two absorbers in series it has been shown that one absorber completely removes all the ozone from the air sample. This method is stated not to be subject to interference from low concentrations of nitrogen dioxide, but it is alleged that at 100 p.p.m. nitrogen dioxide gives a significant reaction.

Ozone and Nitrogen Dioxide.—The nitrogen dioxide concentration in the test atmosphere was determined at the sampling point on the air exit tube of the exposure chamber. The method used was that of Patty and Petty (1943); these authors state that ozone may interfere by oxidation of the nitrite produced to nitrate, but it is evident from the balance sheet between the concentrations of ozone, nitrogen dioxide, and nitrogen pentoxide, which are given in Table 3 and discussed below, that if such an interference exists it cannot be regarded as serious. The initial concentration of nitrogen dioxide fed into the air stream was determined by analysing the air before the ozone supply was connected. From the difference between these two results the amount of nitrogen dioxide reacting with ozone was determined.

Where the nitrogen dioxide content of the mixture was of the order of 10 p.p.m. or less, the ozone concentration was measured during exposure as described above. At the end of the experiment the nitrogen dioxide feed was stopped, and, after an appropriate period for flushing out the apparatus, the ozone concentration was again measured. The difference between these two values gave the amount of ozone reacting with the nitrogen dioxide.

When the nitrogen dioxide concentration was much in excess of 10 p.p.m. it interfered with the direct estimation of the ozone concentration during exposure and the values in Table 4 enclosed in brackets have been obtained by subtracting from the measured initial ozone concentration an amount equivalent to one-half the measured decrease in nitrogen dioxide, expressed in p.p.m. This procedure assumes that the decrease in ozone concentration is due to the reaction of 1 molecule of ozone with 2 of nitrogen dioxide; an inspection of those experiments in Table 3 where both the ozone and nitrogen dioxide losses have been measured suggests that the procedure is inferior to a direct determination of ozone concentration, but that it is not likely to introduce errors which will invalidate any of the conclusions.

The analytical techniques used give their answer in terms of mg./m.^{3} air. In this paper the usual calculation has been applied to convert these figures into parts per million by volume (p.p.m.), a procedure which is open to theoretical objection but which permits the reaction of ozone and nitrogen dioxide on a molar basis to be readily apparent.

Nitrogen Pentoxide.—The nitrogen pentoxide content of the test atmospheres was determined by the direct nitration of a 2 : 4 xylenol reagent (Diggle and Gage, 1954). We have found that a nitrogen dioxide atmosphere, prepared as described above, does not, in the absence of ozone, react at all with this reagent. In our previous paper we made the observation that a nitrogen dioxide atmosphere, prepared by the volatilization of a chloroform solution of the substance, is absorbed to a small extent under these conditions; the conclusion must be drawn that nitrogen dioxide can exist in molecular association with chloroform, sufficiently loosely not to interfere with the determination of the substance by the static absorption in Griess-Ilosvay reagent, but, nevertheless, in a manner which permits the partial retention of the vapour in the xylenol reagent.

Toxicity of Ozone

Single Exposures.—Table 1 shows the effect of a single four-hour exposure of a range of concentrations of ozone on rats and Table 2 is a summary of similar experiments on mice.

TABLE 1

EFFECT ON RATS OF SINGLE FOUR-HOUR EXPOSURE TO OZONE

Concentration (p.p.m.)	Rats			Effects
	No.	Sex	Mean Weight (g.)	
3·4	3	F	150	Laboured breathing towards end of exposure, complete recovery
3·6	4	M	202	As above
8·0	4	M	182	Dyspnoea after 2 hours, becoming severe; 1 death within 24 hours of exposure
9·0	3	F	160	Dyspnoea after 2 hours, becoming severe; no deaths
14·0	3	F	160	Dyspnoea and lethargy after 30 minutes; all died during exposure
17·0	4	M	195	Acute dyspnoea after 2 hours; 3 died during exposure, 1 later
30–36	4	M	188	Acute dyspnoea after 2 hours; all died during exposure

TABLE 2

EFFECT ON MICE OF SINGLE FOUR-HOUR EXPOSURE TO OZONE

Concentration (p.p.m.)	Mice			Effects
	No.	Sex	Mean Weight (g.)	
9	6	F	20	Dyspnoea developed during exposure, severe in 3 mice which died within 24 hours of exposure
12·7	5	F	20	Dyspnoea rapidly became severe, 2 died during exposure, remainder died within 24 hours
16·5	7	F	20	As above, 3 died during exposure, remainder within 24 hours
24	5	F	20	As above, all died during exposure

The effect of the gas on both species is similar; the results do not permit a statistical calculation of a lethal concentration (L.C. 50), but it is most probably in the region of 10 to 12 p.p.m. Concentrations below this may produce signs of transient respiratory distress during the experiment, above this figure the animals become comatose and develop acute dyspnoea which terminates in death during or within 24 hours after the exposure.

Post-mortem examination revealed the lungs distended with oedematous fluid. Histological examination of pulmonary tissue showed extensive

oedema and emphysema, but no haemorrhage or engorgement of alveolar capillaries.

Repeated Exposures.— Six male rats (120 to 140 g.) were exposed to 2·5 p.p.m. ozone for four hours a day for eight days. They suffered no apparent discomfort and gained weight normally. Lungs removed from these animals after death appeared normal and histological examination revealed nothing abnormal.

The experiment was repeated on five male rats (160 to 250 g.) with a 4·5 p.p.m. ozone concentration for 19 days. All of the animals save one survived the experiment and increased in weight normally, though they showed slight respiratory distress towards the end of each four-hour exposure period from which they recovered overnight. During the fifth exposure one of the rats (160 g.) developed dyspnoea which became increasingly severe with successive exposures. It lost weight and died after the twelfth exposure.

On post-mortem examination the lungs of the rats which survived the 4·5 p.p.m. ozone exposures appeared normal, though one showed small oedematous patches on histological examination. In the rat which succumbed during the exposure, the thorax was distended and the lungs very enlarged; two lobes appeared haemorrhagic. On histological examination of the lungs of this animal, there were, in addition to oedema and emphysema, localized areas of sero-fibrinous haemorrhagic exudate, enmeshing large numbers of leucocytes.

TABLE 3

REACTION OF OZONE AND NITROGEN DIOXIDE TO PRODUCE NITROGEN PENTOXIDE

Ozone (p.p.m.)		NO_2 (p.p.m.)		N_2O_5 (p.p.m.)			% N_2O_5 Found	
Before Mixing	After Mixing	Before Mixing	After Mixing	Calculated from O_3 Loss	Calculated from NO_2 Loss	Measured	On Ozone Loss	On NO_2 Loss
5·6	5·9	5·6	1·8	0	1·9	0	—	—
5·2	5·0	9·8	4·75	0·2	2·5	0·31	155	12·4
11·5	10·7	4·75	2·1	0·8	1·3	0·31	38·8	23·8
9·9	8·9	4·1	2·9	1·0	0·6	0·44	44·0	73·3
9·2	8·0	11·1	5·75	1·2	2·7	0·84	70·0	31·1
10·8	9·1	4·2	2·2	1·7	1·0	0·88	51·8	88·0
11·9	9·2	9·9	3·9	2·7	3·0	0·94	34·8	31·4
9·0	5·6	10·4	3·9	3·4	3·2	1·4	41·2	43·8
10·2	—	20·4	12·5	—	7·0	1·9	—	27·1
6·7	—	22·2	11·5	—	5·3	2·94	—	55·5
6·5	—	40·0	27·0	—	6·5	3·38	—	52·0
7·6	—	33·4	21·6	—	5·9	3·38	—	57·2

TABLE 4

EFFECT ON RATS (200–250 g.) OF SINGLE FOUR-HOUR EXPOSURE TO MIXTURES OF OZONE AND NITROGEN DIOXIDE

Ozone (p.p.m.)	NO_2 (p.p.m.)	N_2O_5 (p.p.m.)	Total Equivalent Ozone Concentration (p.p.m.)	Rats		Effects
				Sex	No.	
5·9	1·8	0	5·9	M	3	Slight dyspnoea, no deaths
5·0	4·75	0·31	5·9	M	3	Slight dyspnoea, no deaths, lungs normal
5·6	3·9	1·4	9·8	M	3	Dyspnoea, lethargy, no deaths
(1·3)	11·5	2·94	10·1	F	3	Lethargy, dyspnoea becoming acute in 1 rat which died within 24 hours with intense oedema and emphysema
(0)	27·0	3·38	10·1	M	3	Dyspnoea and lethargy, no deaths but patches of oedema and emphysema in lungs
8·9	2·9	0·44	10·2	F	3	As above
8·0	5·75	0·84	10·5	F	3	Severe dyspnoea, all died within 24 hours with extensive oedema and emphysema
(1·25)	21·6	3·38	11·4	F	3	Dyspnoea and lethargy, no deaths, patches of oedema and emphysema in lungs
10·7	2·1	0·31	11·6	F	3	As above
(6·0)	12·5	1·9	11·7	F	3	Dyspnoea, one died within 24 hours, lung oedema and emphysema
9·1	2·2	0·88	11·7	M	3	Dyspnoea, 1 died during exposure, 1 within 24 hours; lung oedema
9·2	3·9	0·94	12·0	M	3	Acute dyspnoea, all died within 24 hours; extensive oedema and emphysema in lungs

Ozone and Nitrogen Dioxide

Production of Nitrogen Pentoxide.—Table 3 is a summary of the analytical results on a series of atmospheres containing ozone and nitrogen dioxide.

From the decrease in the concentrations of ozone and nitrogen dioxide, which results from the admixture and which have been calculated as described in a previous section, are derived the expected nitrogen pentoxide concentrations, according to the equation $2NO_2+O_3=N_2O_5+O_2$. These concentrations calculated from the ozone and nitrogen dioxide losses are in fairly good agreement with one another at the higher nitrogen pentoxide concentrations. The higher analytically determined nitrogen pentoxide concentrations approach to one-half of the expected concentrations, and this was the approximate value given in our previous paper for the fraction which could be determined analytically of a nitrogen pentoxide atmosphere generated from a chloroform solution and brought into contact with experimental animals.

Toxicity.—A summary of the toxicological effects on rats of single exposure to the ozone-nitrogen dioxide atmospheres is given in Table 4. Included in this Table is a column headed "total equivalent ozone concentration". These figures are based on the observation that while the acute toxic action of ozone is similar to that of nitrogen pentoxide, the latter is about three times more active than the former ; the measured ozone concentration has been added to three times the measured nitrogen pentoxide concentration to give the total equivalent ozone concentration.

The individual experiments listed in the Table have been arranged in increasing order of total equivalent ozone concentration. The general pattern of symptoms produced by these mixed atmospheres resembled that noted for ozone and for nitrogen pentoxide ; with low concentrations there was mild respiratory distress, with increasing concentrations the rats became rather comatose and as the lethal concentrations were approached acute gasping dyspnoea developed, terminated by death either during exposure or delayed. Histological examination of the lungs of affected animals revealed oedema and emphysema and some congestion of the alveolar capillaries, but no haemorrhage.

Discussion

The experimental investigation of the acute toxicity of pure ozone to rats and mice has indicated that the L.C. 50 under our experimental conditions is of the order of 10 to 12 p.p.m. This figure is considerably lower than that arising from Thorp's (1941) work and agrees with the higher toxicity reported by Witheridge and Yaglou (1939).

The lower safe limit for limited repeated exposures to rats is between 2·5 and 4·5 p.p.m. Stokinger (1954) quotes a much lower figure from McDonnell's work, but this investigator used guinea-pigs and the experiments lasted far longer and the mortalities recorded were due to the development of pneumonia. In our experiment at 4·5 p.p.m. ozone, the one death was probably due to pneumonic infection and it may well be that the chronic toxicity of ozone derives in large part from an increased susceptibility to lung infection.

The general pattern of symptoms and the changes in pulmonary tissue produced by ozone are very similar to those previously reported for nitrogen pentoxide. The L.C. 50 values of the two substances are of the order of 10 to 12 p.p.m. and 3 to 4 p.p.m., which indicates that nitrogen pentoxide has about three times the acute toxicity of ozone.

The analytical figures on the atmospheres containing both ozone and nitrogen dioxide leave no doubt that the two components react in part to form nitrogen pentoxide ; there is an approximate equivalence between the loss of ozone and twice the loss of nitrogen dioxide and this figure is of the same order as the production of nitrogen pentoxide when the known loss of this substance under the experimental conditions is taken into consideration. These observations are in accord with the chemical reaction $2NO_2 + O_3 = N_2O_5 + O_2$. The analytical results are not sufficiently precise or extensive to permit a calculation of the rate and equilibrium constants of the reaction, but it appears that the production of nitrogen pentoxide is a function of the initial concentrations of both components.

The effects produced by exposing rats to atmosphere containing both ozone and nitrogen dioxide demonstrate clearly that the toxicity of the mixture is greater than would be anticipated from the toxicity of the components. This apparent synergism can be satisfactorily attributed to the reaction producing nitrogen pentoxide, whose physiological action is very similar to that of ozone, and the effects of the two appear quantitatively to be additive. If to the measured ozone concentration is added three times the nitrogen pentoxide concentration to give a "total equivalent ozone concentration", the L.C. 50 calculated on this basis is of the same order as that for ozone alone, and for a given total equivalent ozone concentration the toxicity is largely irrespective of whether ozone or nitrogen pentoxide is the major toxic component.

Our experiments have demonstrated that although the toxicity of an ozone atmosphere can be increased

oedema and emphysema, but no haemorrhage or engorgement of alveolar capillaries.

Repeated Exposures.— Six male rats (120 to 140 g.) were exposed to 2·5 p.p.m. ozone for four hours a day for eight days. They suffered no apparent discomfort and gained weight normally. Lungs removed from these animals after death appeared normal and histological examination revealed nothing abnormal.

The experiment was repeated on five male rats (160 to 250 g.) with a 4·5 p.p.m. ozone concentration for 19 days. All of the animals save one survived the experiment and increased in weight normally, though they showed slight respiratory distress towards the end of each four-hour exposure period from which they recovered overnight. During the fifth exposure one of the rats (160 g.) developed dyspnoea which became increasingly severe with successive exposures. It lost weight and died after the twelfth exposure.

On post-mortem examination the lungs of the rats which survived the 4·5 p.p.m. ozone exposures appeared normal, though one showed small oedematous patches on histological examination. In the rat which succumbed during the exposure, the thorax was distended and the lungs very enlarged; two lobes appeared haemorrhagic. On histological examination of the lungs of this animal, there were, in addition to oedema and emphysema, localized areas of sero-fibrinous haemorrhagic exudate, enmeshing large numbers of leucocytes.

TABLE 3

REACTION OF OZONE AND NITROGEN DIOXIDE TO PRODUCE NITROGEN PENTOXIDE

Ozone (p.p.m.)		NO_2 (p.p.m.)		N_2O_5 (p.p.m.)			% N_2O_5 Found	
Before Mixing	After Mixing	Before Mixing	After Mixing	Calculated from O_3 Loss	Calculated from NO_2 Loss	Measured	On Ozone Loss	On NO_2 Loss
5·6	5·9	5·6	1·8	0	1·9	0	—	—
5·2	5·0	9·8	4·75	0·2	2·5	0·31	155	12·4
11·5	10·7	4·75	2·1	0·8	1·3	0·31	38·8	23·8
9·9	8·9	4·1	2·9	1·0	0·6	0·44	44·0	73·3
9·2	8·0	11·1	5·75	1·2	2·7	0·84	70·0	31·1
10·8	9·1	4·2	2·2	1·7	1·0	0·88	51·8	88·0
11·9	9·2	9·9	3·9	2·7	3·0	0·94	34·8	31·4
9·0	5·6	10·4	3·9	3·4	3·2	1·4	41·2	43·8
10·2	—	20·4	12·5	—	7·0	1·9	—	27·1
6·7	—	22·2	11·5	—	5·3	2·94	—	55·5
6·5	—	40·0	27·0	—	6·5	3·38	—	52·0
7·6	—	33·4	21·6	—	5·9	3·38	—	57·2

TABLE 4

EFFECT ON RATS (200–250 g.) OF SINGLE FOUR-HOUR EXPOSURE TO MIXTURES OF OZONE AND NITROGEN DIOXIDE

Ozone (p.p.m.)	NO_2 (p.p.m.)	N_2O_5 (p.p.m.)	Total Equivalent Ozone Concentration (p.p.m.)	Rats		Effects
				Sex	No.	
5·9	1·8	0	5·9	M	3	Slight dyspnoea, no deaths
5·0	4·75	0·31	5·9	M	3	Slight dyspnoea, no deaths, lungs normal
5·6	3·9	1·4	9·8	M	3	Dyspnoea, lethargy, no deaths
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Our experiments have demonstrated that although the toxicity of an ozone atmosphere can be increased

by the presence of oxides of nitrogen, this effect is not significant until the nitrogen oxide concentration approaches that of ozone, when the components are brought into contact at room temperature. We have confirmed in other experiments the observations of other investigators by showing that the usual pattern of ozonizer, operating by a silent electrical discharge on fairly dry air, produces only a negligible trace of nitrogen oxides and therefore nitrogen pentoxide plays no part in the toxicity of an atmosphere so produced. Thorp (1941), however, using a spark discharge, has maintained that he has achieved a mixture in which the nitrogen oxides are present in nearly the same concentration as ozone. It would be interesting and profitable to investigate the nitrogen pentoxide production under such conditions; we ourselves have had the opportunity of making analytical measurements in an insulator testing establishment where there was an evident evolution of ozone in the vicinity of a brush electrical discharge. We have found that an ozone concentration of 2·2 p.p.m. is accompanied by a nitrogen pentoxide concentration of 0·25 p.p.m. These figures indicate that in this atmosphere ozone is the chief toxic hazard, yet the concentration of nitrogen pentoxide, equivalent to 0·75 p.p.m. ozone, is not to be neglected. The nitrogen dioxide concentration was found to be of the order of 1 p.p.m. and did not contribute to the toxicity.

The concentration of ozone which has been recommended by the American Conference of Governmental Industrial Hygienists (1954), not to be exceeded in a factory where men are continually exposed, is 0·1 p.p.m. and the present investigation suggests that it is not unreasonable. We have shown that the assessment of the hazard of an ozone atmosphere by means of ozone determination would be adequate if the ozonization derived from a silent electrical discharge, but it might be misleading when atmospheres produced by spark discharge or other methods are involved.

Summary

The concentration of ozone which causes 50% mortality to rats and mice exposed for one period of four hours has been found to be in the region of 10 to 12 p.p.m. The cause of death is acute pulmonary oedema.

A limited number of repeated four-hour exposures on rats at 4·5 p.p.m. causes respiratory distress and the death of one rat, probably due to pneumonic infection. Repeated exposures at 2·5 p.p.m. have no effect.

Dilute mixtures of ozone and nitrogen dioxide in air react in part to give nitrogen pentoxide, the amount produced depending on the concentrations of the reactants. The toxic effects of ozone and nitrogen pentoxide are qualitatively similar, though the latter is about three times as active as the former. The effects are additive and the observed increase in the toxicity of an ozone atmosphere brought about by the presence of oxides of nitrogen can be adequately attributed to the nitrogen pentoxide present.

The effect of these observations on the assessment of the toxic hazard from industrial ozone concentrations is discussed.

We wish to express our indebtedness to Dr. M. W. Goldblatt for advice and to Mr. J. Crozier for technical assistance.

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THE CONSTRUCTION OF CRITICAL ORIFICES WORKING WITH SMALL PRESSURE DIFFERENCES AND THEIR USE IN CONTROLLING AIRFLOW

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The use of the critical orifice to stabilize the flow rate of a gas is well known. It has been used, for example, in environmental studies in industrial hygiene to stabilize the flow of air through sampling circuits, while in the impinger the impaction jet can be run under "critical flow" conditions to give a sonic jet for impaction purposes and at the same time a controlled sampling rate.

Many authors have investigated experimentally and theoretically the discharge of gas through an orifice. Saint-Venant and Wantzel (1839) first obtained the equations of discharge by assuming that an adiabatic type of pressure-volume relationship was applicable under the conditions of flow. They obtained the relationships :—

$$u^2/2 = \frac{\gamma}{\gamma-1}\,\frac{P_o}{\rho_o}\left\{1-\left(P/P_o\right)^{\frac{\gamma-1}{\gamma}}\right\} \quad \ldots\ \ldots \quad (1)$$

$$w = A\sqrt{\frac{2\gamma}{\gamma-1}P_o\,\rho_o\left(P/P_o\right)^{2/\gamma}\left\{1-\left(P/P_o\right)^{\frac{\gamma-1}{\gamma}}\right\}} \quad (2)$$

in which u is the speed of the gas, ρ its density, P the pressure in the jet, A its area, and w the mass rate of discharge. The suffix o refers to conditions inside the discharging vessel in which u = o.

Saint-Venant and Wantzel observed that the equation (2) gave a maximum value for w when $P = P_o\left(\frac{2}{\gamma+1}\right)^{\frac{\gamma}{\gamma-1}}$ and that as P tended towards zero w also became vanishingly small, *i.e.*, the equation predicted zero rate of gaseous discharge into a vacuum. Experimental investigation of this paradoxical conclusion showed that the rate of discharge increased as the ratio of $\frac{\text{receiver pressure (Pr)}}{\text{Po}}$ decreased from 1 to about 0·4, but that after that it remained constant. They concluded that the pressure in the jet and in the receiver were not the same for $o < \frac{Pr}{P_o} < 0{\cdot}4$.

The theoretical consideration of discharge under critical conditions was developed by Reynolds (1886). He assumed that once critical flow had been established w (Eq. 2) remained constant but that A varied. The condition for minimal area of the jet led to the condition $P = Po\left(\frac{2}{\gamma+1}\right)^{\frac{\gamma}{\gamma-1}}$ which implies that the velocity in the minimal section is that of sound under the conditions of pressure and temperature there pertaining. The discharge of gas through an orifice under critical conditions can therefore be regarded as consisting of a number of streams originating in the discharging vessel, which contract and pass through the minimal section or throat, and subsequently behave in a manner which enables the emerging streams to come to equilibrium with the pressure in the receiver. Reynolds deduced that when the velocity of sound was attained in the throat it would be impossible for waves of condensation to travel from the receiver back into the throat, and, therefore, variations in receiver pressure would not affect the rate of discharge, provided the receiver pressure Pr was less than the theoretical figure of 0·527 Po. This conclusion is in agreement with the experimental observations of Saint-Venant and Wantzel.

A series of most elegant experiments was carried out by Hartshorn (1918), following the suggestion of Lord Rayleigh, to test whether the criterion of

critical flow Pr $<$ 0·527 Po held for orifices of various types. His experimental technique enabled him to record flow changes of less than 0·1%, and he found that the theoretical criterion Pr $<$ 0·527 Po only applied to convergent orifices. Parallel-sided orifices did not give constant flow for values of Pr $>$ 0·2 Po while divergent cones gave constant flow for values of Pr/Po from 0·2 to 0·8 according to the angle of the cone. The change in flow with pressure above the critical value was usually very small at first; for example, with a parallel-walled orifice, Hartshorn showed that critical flow is attained when 0·18 $<$ Pr/Po $<$ 0·22 while the flow rate reaches 99% of the critical flow when Pr/Po = 0·44.

The subject was further developed by Stanton (1926) who investigated the velocity distribution in various configurations of jets both by the Pitot tube method and by means of "shadow" photography. He found that in all cases the section of the air jet diminished to a minimal value and then expanded, and that the velocity through this minimal section was that of sound under the conditions existing. The minimal section in the case of a free jet is not constant in area or position relative to the plane or throat of the orifice but depends on the total ratio of the expansion. This effect explains the initial small change of flow with pressure in Hartshorn's experiments. In the case of diverging nozzles he found that the minimal section could, for all practical purposes, be regarded as coincident with the throat of the nozzle.

Control Orifices with Divergent Cones

The experiments described in this paper were made to obtain data for the design of low-pressure-drop control orifices and to investigate methods of fabrication and calibration. These orifices were required to control the airflow in a wind tunnel for the study of airborne infection (Druett and May, 1952). For this reason, the orifices studied were in the flow range of 10 to 200 l./min. No attempt was made to emulate the extreme precision of Hartshorn's experiments. Flow rates were measured on a rotameter with which it was possible to detect flow changes with an accuracy of 0·5%. For this reason the reservoir pressures recorded for the onset of critical flow are somewhat higher than those given by Hartshorn.

The factors investigated were:

(1) The pressure drop necessary to produce critical flow with various cone angles; (2) the effect of cone length on the pressure drop necessary to produce critical flow with orifices of various sizes; and (3) the design of the entry to the throat section.

Material

All orifices were made from perspex. This material was chosen on the grounds of transparency, availability, free working properties, and the ease with which a highly polished finish can be obtained.

Method of Construction

Reamers were made by grinding previously hardened steel to the required taper and grinding flats to form a two-edged cutter. Subsequently a D-cutter was tried and proved to be highly successful. It was found impossible to shape the steel before hardening owing to the subsequent distortion of the metal by heat.

A piece of perspex rod about 3 cm. long was drilled axially and one end radiused to form a smooth entry. The cutter of the appropriate angle was then inserted from the opposite end of the rod and work continued until only a short parallel section about 1/10 in. long remained. The coned portion was then polished, the perspex rod reversed in the chuck, and the parallel throat and radiused entrance polished.

Method of Test

The circuit used in these experiments is shown in Fig. 1. Air was drawn through the rotameter and critical orifice under test into a reservoir. The reservoir was continuously evacuated by a pump, the reservoir pressure being adjusted by allowing the air to enter

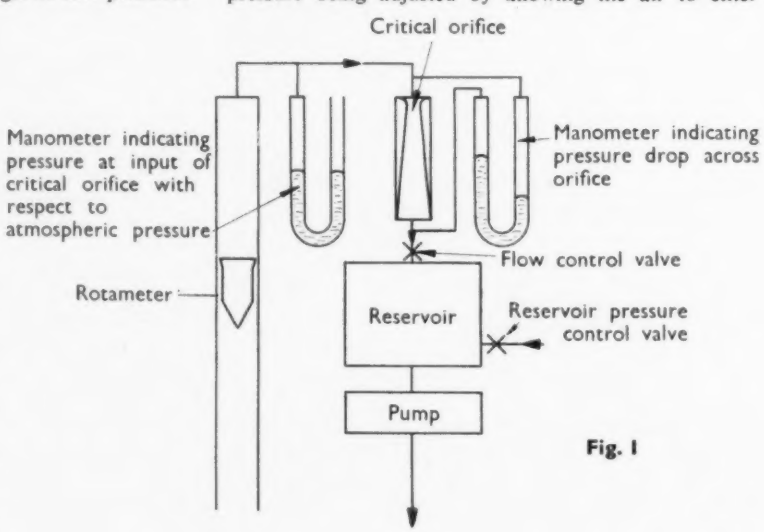

Fig. 1

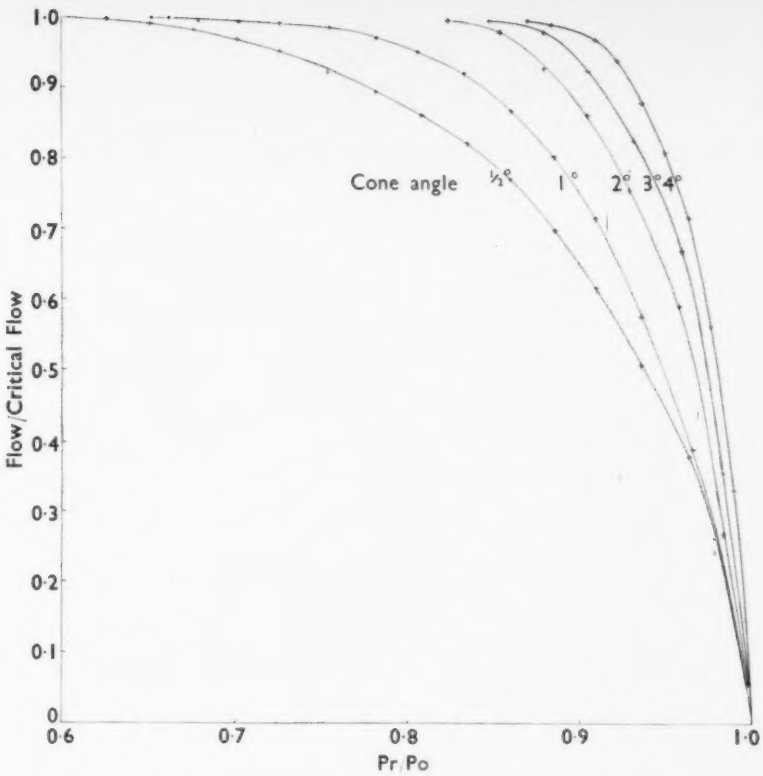
Cone angle ½° 1° 2° 3° 4°
Flow/Critical Flow
1·0
0·9
0·8
0·7
0·6
0·5
0·4
0·3
0·2
0·1
0
0·6
0·7
0·8
0·9
1·0
Pr/Po

Fig. 2

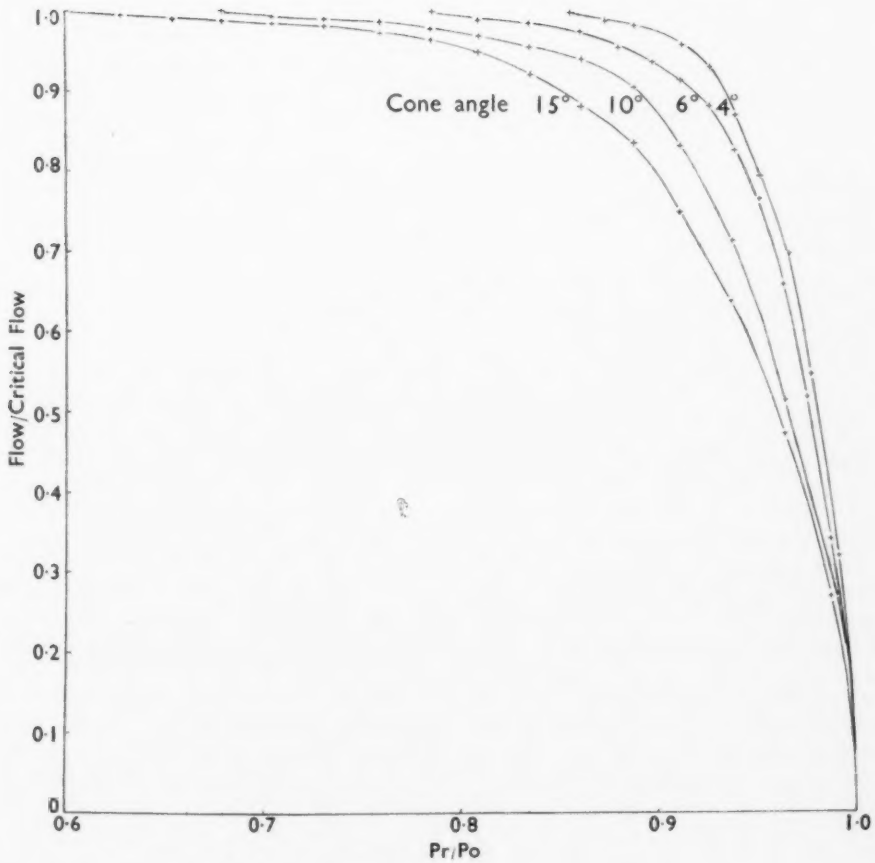
Cone angle 15° 10° 6° 4°
Flow/Critical Flow
1·0
0·9
0·8
0·7
0·6
0·5
0·4
0·3
0·2
0·1
0
0·6
0·7
0·8
0·9
1·0
Pr/Po

Fig. 3

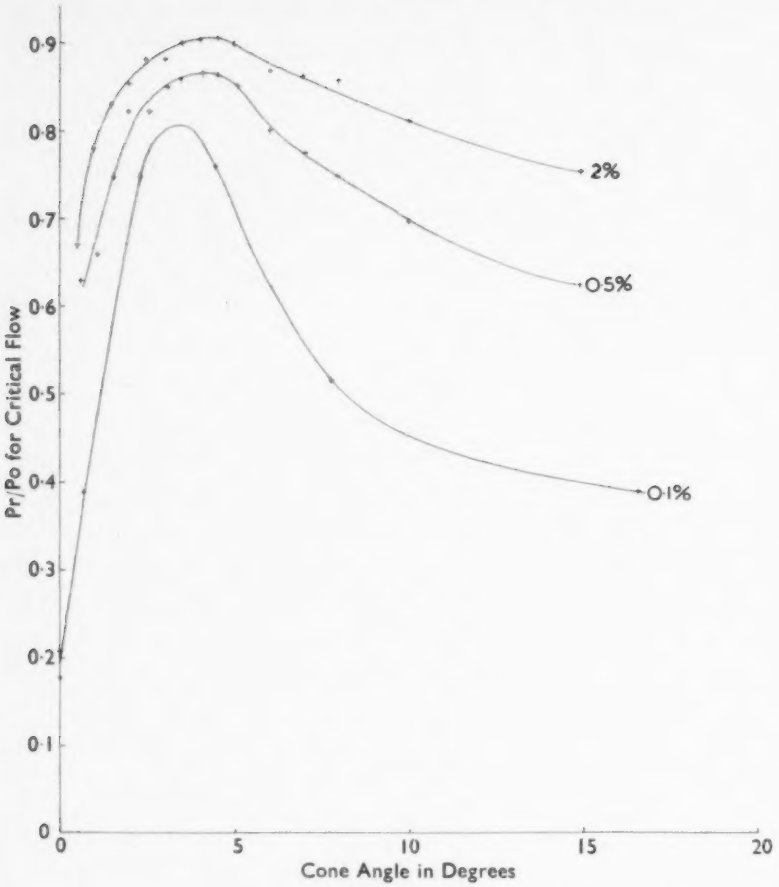

Fig. 4

through the reservoir pressure control valve Fine adjustment of the pressure drop across the orifice was made by means of the flow control valve. A series of readings of flow rate and pressure drop was taken, and the flow rate corrected to normal pressure.

Results

Pressure Drop : Flow Characteristics.—Orifices were made with divergent sections having the following total angles ½°, 1°, 1½°, 2°, 2½°, 3°, 3½°, 4°, 4½°, 5°, 6°, 7°, 8°, 10°, and 15° and the flow rates determined for various pressure drops across each orifice. These results were plotted as shown for representative cases in Figs. 2 and 3. Except for values of flow/critical flow near to unity, the curves obtained were found to approximate to the first quadrants of a family of ellipses whose semi-axes have Pr/Po = 1 and flow/critical flow = 1 as common tangents whose centre lies on the abscissa, *i.e.*, of the form $(x - 1 + a)^2 + a^2 y^2 = a^2$ where $o < a < 1$. This is as theoretical considerations predict (Prandtl, 1936). From these results a curve of total cone angle against pressure drop for critical flow was plotted, as shown in Fig. 4. This curve shows a sharp maximum at 4° and this angle therefore represents the optimal value for low-pressure-drop critical orifices.

Length of Conical Part of Orifice.—For these experiments three orifices were made with a total cone angle of 4° having flow rates of 20 l./min., 104 l./min. and 200 l./min. respectively. A fiducial ring was made on the outside of the perspex round each orifice approximately in the plane of intersection of the conical section with the cylindrical throat. From this fiducial ring distances were marked at appropriate intervals along the venturi section of the orifice. A series of readings was taken of the minimal pressure drop across each orifice to give critical flow with the conical section cut to each of the chosen lengths in turn. Finally, a longitudinal section was made through the axis of each orifice, and the distance from the plane of the fiducial ring to that of the plane of intersection of the conical section with the throat was determined by means of a travelling microscope. A plot was made of cone length against minimal pressure drop for critical flow as shown in Fig. 5.

For short lengths of cone, the experimental curves approach those derived by applying the equation of continuity to the venturi section taking conditions pertaining in the throat as the boundary conditions (Prandtl, 1936). Curves A and B of Fig. 5 were derived from the equation of continuity for 100 l./min. and 200 l./min. respectively. It was found that increasing the length of the orifice throat increased the pressure drop necessary for critical flow, due to increased frictional losses. The throat length was therefore kept as short as possible. It is probable that small defects in machining or

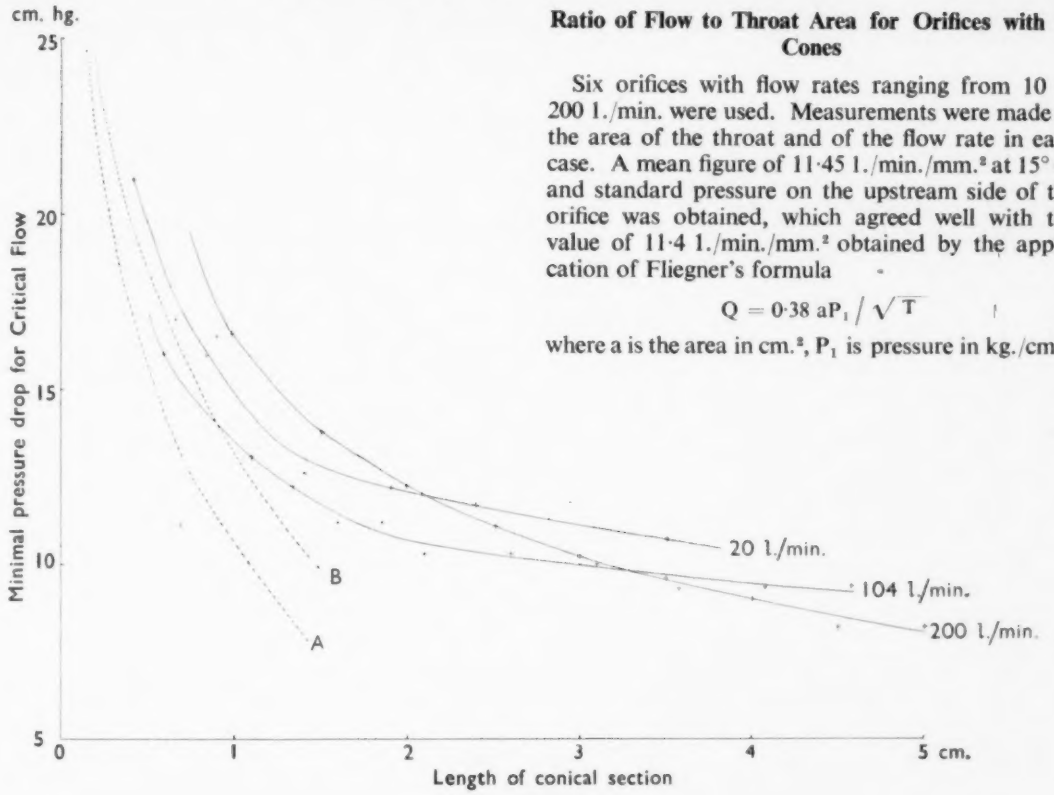

Fig. 5

polishing may also have introduced frictional losses, and so the curves given in Fig. 5 can be taken as approximate only. Calculations based on the equation of continuity predict that the length of conical orifice necessary to give any chosen critical pressure will increase in proportion to the radius of the throat, *i.e.*, proportional to the square root of the flow. On the other hand, since the frictional wall loss is proportional to the radius of the throat, and the rate of discharge is proportional to the area of the throat, the frictional losses per unit mass of gas discharged will decrease inversely as the throat diameter.

These generalizations offer an explanation of the shapes of the experimental curves in which we observe that the lowest critical pressure is obtained for the highest flow rate in the case of a long venturi, but that an ordered sequence is not obtained for the other flow rates for short venturis.

Entrant Shape.—A variety of entrant shapes was tried, the most satisfactory types being those formed by radiusing the walls to give a continuous smooth curve into the throat.

Ratio of Flow to Throat Area for Orifices with 4° Cones

Six orifices with flow rates ranging from 10 to 200 l./min. were used. Measurements were made of the area of the throat and of the flow rate in each case. A mean figure of 11·45 l./min./mm.^{2} at 15° C. and standard pressure on the upstream side of the orifice was obtained, which agreed well with the value of 11·4 l./min./mm.^{2} obtained by the application of Fliegner's formula

$$Q = 0{\cdot}38\, aP_1 / \sqrt{T}$$

where a is the area in cm.^{2}, P_1 is pressure in kg./cm.^{2}, T is absolute temperature in °Kelvin, and Q is the output in kg./sec.

Effect of Upstream Pressure

As shown by the Fliegner formula (Prandtl, 1936) the flow through a critical orifice varies directly as the absolute upstream pressure. This was confirmed experimentally with venturi type orifices. As shown in Fig. 6 the "critical" type flow took place at pressure differences of less than one-half the entrant pressure, as would be expected.

Production of Venturi Type Orifices for Control of Gas Flow

The manufacture of orifices for control purposes was carried out as described earlier in this paper. The piece of perspex rod was initially bored with a drill a few thousandths of an inch smaller than the diameter theoretically predicted for the required flow rate. The smooth, radiused entrance and conical portion were then machined and polished. Finally, the throat was enlarged by careful polishing until the required flow rate was registered on the calibrating gasmeter.

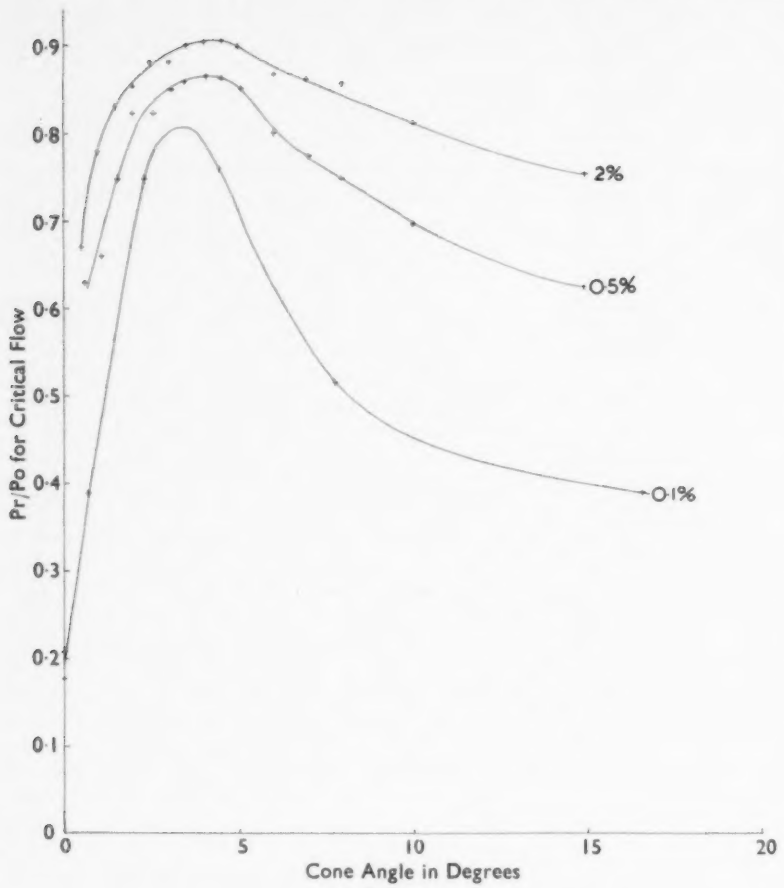

Fig. 4

through the reservoir pressure control valve Fine adjustment of the pressure drop across the orifice was made by means of the flow control valve. A series of readings of flow rate and pressure drop was taken, and the flow rate corrected to normal pressure.

Results

Pressure Drop : Flow Characteristics.—Orifices were made with divergent sections having the following total angles ½°, 1°, 1½°, 2°, 2½°, 3°, 3½°, 4°, 4½°, 5°, 6°, 7°, 8°, 10°, and 15° and the flow rates determined for various pressure drops across each orifice. These results were plotted as shown for representative cases in Figs. 2 and 3. Except for values of flow/critical flow near to unity, the curves obtained were found to approximate to the first quadrants of a family of ellipses whose semi-axes have Pr/Po = 1 and flow/critical flow = 1 as common tangents whose centre lies on the abscissa, *i.e.*, of the form $(x - 1 + a)^2 + a^2 y^2 = a^2$ where $o < a < 1$. This is as theoretical considerations predict (Prandtl, 1936). From these results a curve of total cone angle against pressure drop for critical flow was plotted, as shown in Fig. 4. This curve shows a sharp maximum at 4° and this angle therefore represents the optimal value for low-pressure-drop critical orifices.

Length of Conical Part of Orifice.—For these experiments three orifices were made with a total cone angle of 4° having flow rates of 20 l./min., 104 l./min. and 200 l./min. respectively. A fiducial ring was made on the outside of the perspex round each orifice approximately in the plane of intersection of the conical section with the cylindrical throat. From this fiducial ring distances were marked at appropriate intervals along the venturi section of the orifice. A series of readings was taken of the minimal pressure drop across each orifice to give critical flow with the conical section cut to each of the chosen lengths in turn. Finally, a longitudinal section was made through the axis of each orifice, and the distance from the plane of the fiducial ring to that of the plane of intersection of the conical section with the throat was determined by means of a travelling microscope. A plot was made of cone length against minimal pressure drop for critical flow as shown in Fig. 5.

For short lengths of cone, the experimental curves approach those derived by applying the equation of continuity to the venturi section taking conditions pertaining in the throat as the boundary conditions (Prandtl, 1936). Curves A and B of Fig. 5 were derived from the equation of continuity for 100 l./min. and 200 l./min. respectively. It was found that increasing the length of the orifice throat increased the pressure drop necessary for critical flow, due to increased frictional losses. The throat length was therefore kept as short as possible. It is probable that small defects in machining or

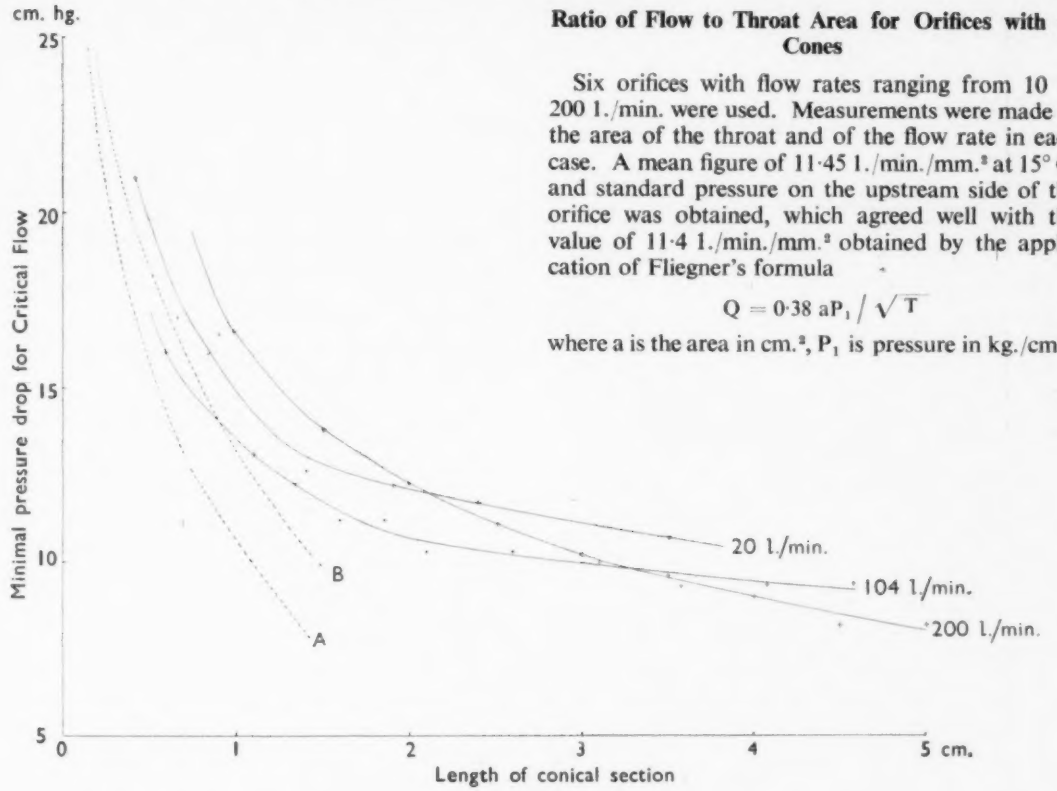

Fig. 5

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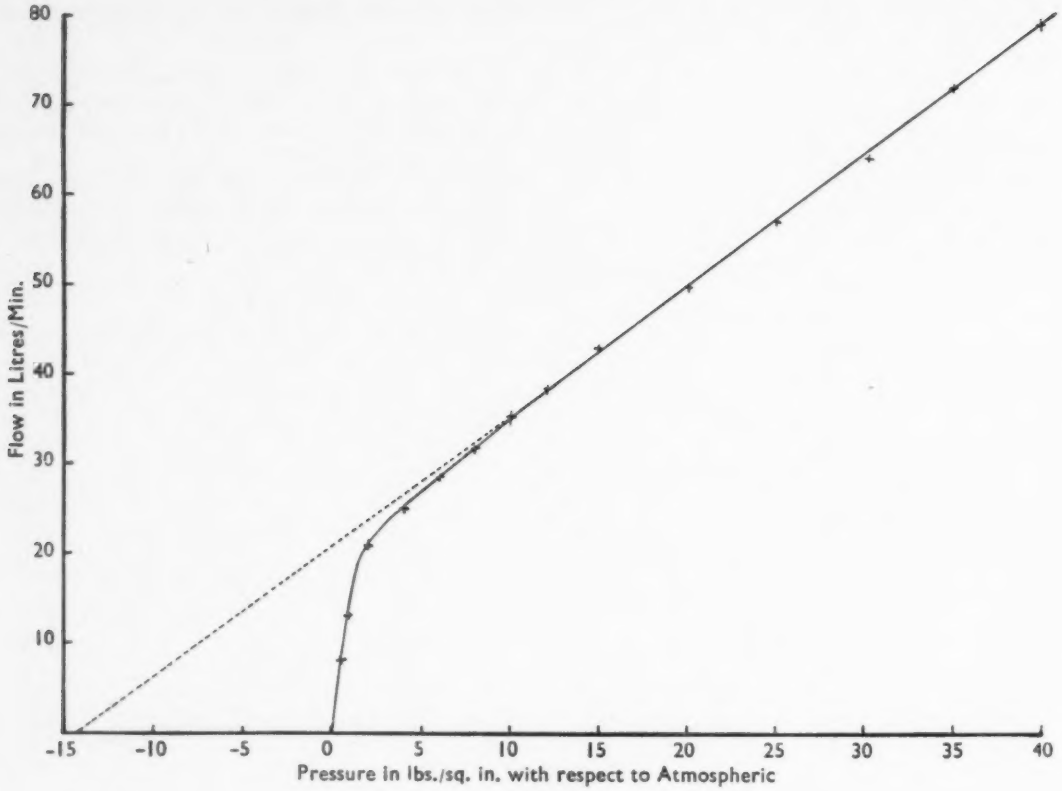

Fig. 6

Conclusion

Orifices of the type described have been in continual use in this department during the past three years and have proved most satisfactory. The use of orifices of this type to stabilize the airflow in aerosol sampling can often lead to a considerable reduction in pump capacity with a consequent saving in both weight and expense. Many visitors have asked for information on the manufacture of these orifices and it was felt that the information contained in this paper, although not novel, might be of general interest.

Summary

A method is described for making and calibrating critical orifices which function at small pressure drops. The critical orifice consists of a parallel throat followed by a divergent conical section. Data are given for the effect of cone length and angle on the characteristics of the orifice.

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MISCELLANEA

The Health Hazards of the Senior Executive

A. R. COOPER

Controller of the North West Merseyside and North Wales Divisions of the British Electricity Authority

The health of a senior executive is essentially a matter for some concern, partly because of the direct effects on the executive himself but also, and probably chiefly, because of the indirect effects on the people under his control.

It is not implied that the decisions of a healthy executive are necessarily better than those of an unhealthy one, for there is no correlation, to my knowledge, between health and wisdom or health and moral values, but it does seem reasonable to assume that an executive will produce his best work if he is not bedevilled by sickness and that his mind will be better able to deal with the problems of his work if it is not being obsessed with real or imaginary troubles of his own.

Arising from these considerations we may ask ourselves how the daily life of the executive varies from the healthy norm (if there is such a standard) and what forms of illness are most frequently recurring with his type.

From the purely biological viewpoint his habits are almost directly opposed to those of a normal healthy animal. He is taken from place to place in a car and sits comparatively motionless throughout his working day. He eats and drinks and smokes far more than any man should and, if it is part of his business to be sociable and to mix pleasantly with people, he may find it very difficult to cut down on these things.

The only really active component in his make-up is his brain and this part of his anatomy is responsible both for controlling the functions of his body and the operation of his business. If the brain is having a very difficult time in dealing with the problems of his business it will not be surprising, at any rate to the layman, if it falls a little short of perfection in the way it handles his body.

The type of executive I had in mind when compiling these notes is the comparatively quiet, conscientious, painstaking man who makes it his business and almost his religion to ensure that the enterprise for which he is responsible shall not fail, that the people engaged in the enterprise shall live happy, creative lives, and that all those who have placed their confidence in his leadership shall never regret it.

The modern tendencies towards large-scale organizations, joint consultation, and worker participation in management have not tended to improve the health of the top executive. These new conditions call for much more self-control, patience, and what is sometimes referred to as " suppressed anger", than was experienced in the days when the manager was expected to " blow off his top " at regular intervals, and such neuroses as existed were allocated to the staff.

Knowing that this situation exists, the question arises, What can be done about it? How can we produce a situation in which a senior executive will tend to be a healthy, efficient individual who is enjoying his work?

In the first place it will be necessary to ensure that he is capable of doing his job without undue stress. If a man accepts a job which is too big for him he will be neither happy nor efficient and as an end-product of these two conditions I would suggest that he is also likely to be unhealthy.

I mention this matter first as there are many men who are driven by overweening ambition, either their own or possibly that of their wives, into thinking that continued promotion is the only measure of success in life. It requires a man of strong character to refuse a promotion even if he knows that he is thoroughly unsuited to the new job. Probably the simplest illustration of this situation is that in which an outstandingly competent fitter is promoted to the rank of foreman in which capacity, instead of directing the work of his own hands, he has to direct the work of others. The result in this case and in others higher up the administrative hierarchy can frequently be disastrous both for the man and the organization. The remedy, as I see it, is for the man to recognize that there is some level appropriate to himself towards which he should strive in the knowledge that he would be rather ashamed to remain below that level and exceedingly unhappy if he tried to operate very far above it. There need be no sense of inferiority in holding any position lower than that of managing director if the aim is to live successfully rather than to struggle for the highest possible salary.

I have laboured this point a little for two reasons ; first, because I think that much misery will come the way of people who are unhealthily ambitious, and, secondly, because I think that a competent executive can do much to allay these symptoms among his staff by treating them essentially as equals who happen to be doing different jobs rather than as the higher and lower forms of life which they may appear to be on the firm's organizational chart.

If now we assume that our executive is the right man for the job what factors emerging from the job are most likely to undermine his health?

I would suggest that frustration is one of the most important. Frustration occurs when action is prevented or impeded. It is usually at a minimum when the executive

can make quick decisions, or when he can obtain quick decisions from others; it is at a maximum when no decisions even on minor matters can be made without lengthy negotiations and references back and forth with higher authorities. The remedy is to delegate authority while knowing that one cannot delegate responsibility. It needs courage on the part of top management and a realization on their part that any man who does a lot of things is certain to do some of them wrongly. The executive is happier and more efficient if he feels that the management are willing to take a chance on his judgment.

The next factor I would bring forward is the worrying or tension-provoking situation which can develop, often quite needlessly, in modern management. The normal ups and downs of any business concern must be accepted with reasonable equanimity (that is one of the qualifications for the job) but there are two major fears which can play havoc with the peace of mind not only of the executive but also with many members of the staff. They are the fear of insecurity and the fear of making mistakes.

Every man is concerned in some degree with the security of his employment. It can be argued that a man who knows his job is safe begins to deteriorate as a certain amount of apprehension is a necessary spur to his activities. This is probably true, but it is also true that no man can give of his best if a series of ruthless dismissals keeps him wondering who goes next and if half his energies are concentrated on looking for other jobs. The solution to this problem is essentially a matter for top management, but it should be appreciated that the climate of opinion which their administration produces can have a significant bearing on the health of the people concerned.

Secondly, there is the fear of doing something wrong. This can become such a powerful disincentive that it can inhibit all those adventuresome and original sorties by which the executive uses his creative genius for the benefit of the firm. He becomes like a batsman whose wicket will never be hit but who will never score any runs. This again is essentially a matter which concerns top management, except that the executive must realize the need to apply lower down the scale the same treatment which we are assuming should be accorded to him.

In all I have so far said I have made no reference to the part which can and probably should be played by the industrial medical officer in these matters. I have deliberately treated the executive as an isolated individual and attempted to indicate some of the forces with which he has to contend in order that the industrial medical officer in recognizing causes will find it a little easier to discover cures.

One thing probably more important to the executive's health than any other, especially if he has no recognized deputy, is that he should have some person to whom he can talk confidentially about anything. Emotional stresses and the inhibitions which may flow from them can often be relieved if the executive can talk about his problems to some person such as the industrial medical officer. He will through force of habit want to talk about his aches and pains, but if he can also talk about the difficulties he is having with A or the troubles which are being caused by disagreements between B and C he will find first, that the answer to many a problem will appear once he has expressed that problem in words, secondly, that tension is relieved by talking about the subject, and thirdly, that the industrial medical officer's knowledge of the personality and emotional backgrounds of the people concerned can sometimes be a great help in working out satisfactory solutions. At this point I feel that I must for his own sake consider the significance of the industrial medical officer in the industrial scheme. It can so easily happen that because of his medical training and the "closed shop" atmosphere which old-fashioned members of the profession have helped to create, he may tend to be somewhat pontifical in his approach to less senior members of the staff and his freedom of association with top management will tend to accentuate this failing. It may be a useful if rather brutal corrective to this attitude to point out that many firms function quite successfully without an industrial medical officer and that even where they exist if a choice had to be made for reasons of economy between discharging either the industrial medical officer or a reasonably competent foreman, the industrial medical officer would almost certainly disappear. No harm will ensue if he carries this thought at the back of his mind, and if it results in his establishing a friendly, informal relationship with every member of the staff from the commissionaire to the general manager it will do much good. Humility of mind is, I think, the answer; the ability to feel towards all members of the staff as an East End parson feels towards his flock, rather than as a country squire used to feel towards his tenants.

And I think that the health of the senior executive would also benefit from considerations of this nature, for I feel sure that an attitude of healthy humility on his part will go a long way towards the creation of a contented mind.

The Health of the Industrial Worker in Iraq*

A. MICHAEL CRITCHLEY

From the Royal Medical College, Baghdad

In Iraq an industrial revolution is in full swing and is advancing more quickly than is fully appreciated. Most Iraqi industrialists have learned from the lessons of history and are not committing all the blunders made by the industrialists of the nineteenth century in Europe.

The biggest and most important industry in Iraq is undoubtedly agriculture, and great efforts are now being made to mechanize and to introduce modern methods of irrigation and fertilization. In England agriculture is one of the healthiest occupations but in Iraq it is the reverse. Iraq is divisible into a number of distinct areas according to the nature of the land, and consequently the crops grown in each zone vary so that the health hazards differ likewise, but it is not exaggerating to state that the average agricultural worker (*fellah*) is a living pathological specimen as he is probably a victim of ankylostomiasis, ascariasis, malaria, bilharzia, trachoma, bejel, and possibly of tuberculosis also. If the various development schemes are allowed to proceed without the advice and wholehearted support and help of the public health specialists and sanitary engineers, such diseases as man-made malaria and bilharzia will spread to areas hitherto free, just as in Egypt.

At the present moment the Iraqi Government Principal Bureau of Statistics is undertaking an industrial survey, and though the results are not available yet, some information can be given. There are approximately 150 firms which employ 50 or more workers, of which the Iraq Petroleum Company is the biggest employer with a pay-roll of over 9,000. In addition, there are many more concerns which employ under 50 persons. Included in the over-50 group of industries are the oil concerns, the weaving and leather manufactures, the brick and cement works, tobacco firms, date packing, cleansing of seeds, and repairs and maintenance of ships. The smaller workshops are extremely varied ranging from the smithies of iron, copper, silver, and gold, to saddle makers, mirror manufacturers, dyers, woolsorters, brush-makers, and tailors.

At present the health authorities do not effectively supervise the workshops, so that child labour is very common. Long hours, including nights, are worked, and frequently the work-places are dirty, badly illuminated, ill ventilated, overcrowded, and equipped with unprotected machinery. The environmental conditions found in some workshops are appalling; for example, in the old tanneries, the copper smithies, the tailors' attics, and the shoemakers' workshops. Naturally the health of the workers in the bad working environment is not satisfactory; bad eyesight, injuries, and illness such as anaemias and tuberculosis are rife, and there is a high incidence of dermatitis.

The dermatological risks in some of the small uncontrolled workshops are well exemplified in the old-fashioned tanneries scattered throughout the country. The contact of the worker's unprotected, bare skin with deleterious solutions is so intimate and prolonged that in spite of the well-known resistance of the dark-skinned to irritants, lesions inevitably develop. Thus in one brief visit to an antiquated tannery in Mosul, I saw more cases of "trade holes" than in 25 years of my professional career. The main lesion is an excoriative, depigmenting and ulcerative dermatitis due to irritation from alkaline solutions used to remove fat from the hides and the subsequent use of chrome. Much less common, but by no means rare, is a malignant pustule contracted mainly by the workers engaged in plucking wool from the sheepskins. In the modern tanneries, which are now replacing the old workshops, these skin hazards are so minimized that dermatitis has become an uncommon occurrence.

A scrutiny of the newer concerns reveals a much rosier position. The biggest employer—the Iraq Petroleum Company—has started off with a health and welfare organization that will bear comparison with that of any other firm in the world. A first-class safety organization has been set up which includes a Safety Committee and a full-time Safety Officer. Therefore, although the presence of hydrogen sulphide in the oil at the main wells at Kirkuk constitutes a risk of the gravest magnitude, yet, owing to the very stringent measures which are being taken to enclose this dangerous oil hermetically from the well-head to the elimination of the gases by burning during the processing of the oil, there are no cases of gas poisoning. Similarly, in the engineering workshops the machines are well sited and guarded, and the shops clean, well-lit, and ventilated. The workers are medically examined before and during employment, are supplied with good canteens, and houses are available for employees of all grades. The sick and injured are cared for in three modern and well-equipped hospitals with 175 beds.

Other Iraqi industrial concerns, *e.g.*, the Iraq Spinning and Weaving Co., the Vegetable Extraction Co., the Bata Shoe Co., have not been slow to follow the good example of the I.P.C. It is of interest to note here that, so far, no cases of byssinosis have been detected amongst the cotton workers employed at the Iraqi Spinning and Weaving Co. This is probably due to two factors: first, length of exposure to cotton dust has not been sufficiently long, and, secondly, this concern being a recent development, the management is employing every modern device to reduce to the minimum the dust in the cardrooms and other parts of the factory. As these firms are situated near large Government hospitals, there is no need for the provision of hospital beds, and the doctors are part-time only, attending for a few hours daily and in emergencies.

Porters are a common, interesting and picturesque feature of Baghdad life, and I investigated a sample group of 100 taken at random from railway yards,

* This paper is based on one delivered to the U.N. Fourth Social Welfare Seminar for Arab States.

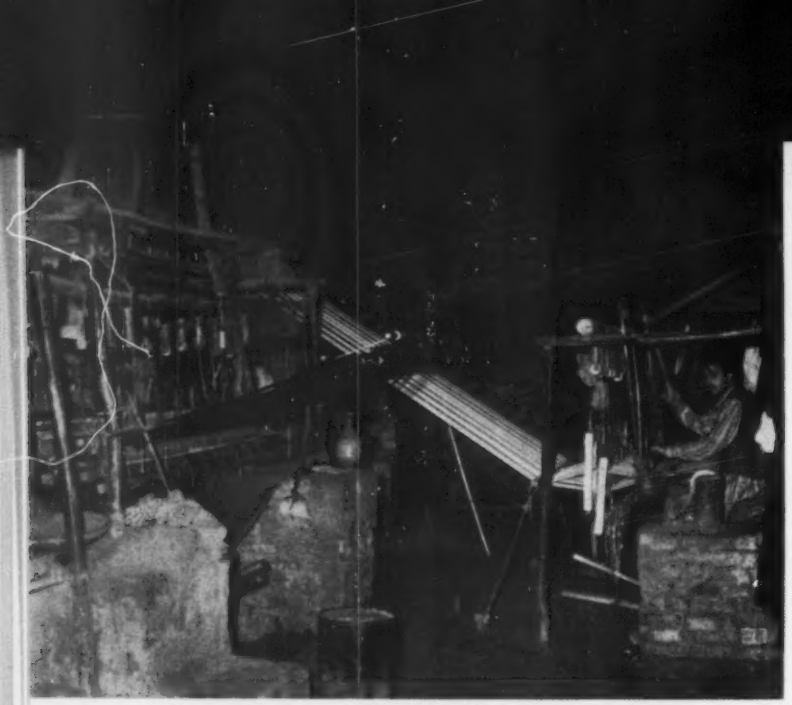

FIG. 1.

FIG. 1.—Old-fashioned loom, now being replaced by the most modern types.

FIG. 2.—Softening process in a modern tannery.

FIG. 3.—Softening process in an old tannery.

FIG. 4.—Wool sorting.

FIG. 2.

FIG. 3.

FIG. 4.

wharves, a factory, and from the heart of the "souk" or bazaar. To understand the existence of this group of workers it is necessary to realize that although, during the past few years since the formation of the Development Board, Baghdad has entered a period of rapid modernization, yet a considerable portion of the business area, especially in the vicinity of the Tigris, remains a district of narrow, tortuous, and uneven passages, low archways opening into Turkish-style courtyards, interspersed with irregular stone steps. Thus this territory is quite unsuited for wheeled traffic and all loads to and from business premises must be carried either by the porters or on the backs of donkeys, mules, or horses.

Over 60% of the porters examined were not Iraqi, but came from Luristan, a Kurdish district in Iran. Their profession is familial, so that up to 14 years of age 38% of all porters remain at home employed in agricultural pursuits, then migrate to Baghdad to become porters, remaining so for the rest of their lives. They probably return for a period of a few weeks each year (usually at harvest time) to their families in Persia where they keep their wives if they are married.

In the group reviewed other porters were found to have been at some period of their lives brick workers (14%), servants, waiters, soldiers, etc. Each man was asked his age, but it was found that no absolute reliance could be placed upon their replies, for they have a vague conception of time and do not possess birth certificates. Their ages were recorded to range from 14 years (employed as a porter for two years) to 70 years. A youth on starting work begins with loads of approximately 50 kg., but as he gains physique, strength, and skill his loads are increased so that it is found that an adult normally carries weights of 200 kg.; some have been known to handle over half a ton, being paid extra money for very awkward loads.

The reason for the ability of a porter to handle such enormous loads is that from the start of his work he adopts a method of handling and carrying which is physiologically sound.

Porters examined had been working for periods varying from three months to 50 years, so that it was possible to assess the effects of such an onerous task. The ill effects found were surprisingly few; thus 9% varicose veins, 4% arthritis of the spinal column, 6% hernia, 3% heart disease. Blood pressure was low (it is commonly low in Iraq) and the highest systolic pressure recorded was 160 and the lowest 90, with an average of 120 mm. Hg.

Nearly all the workers had a mild keratotic condition of the skin over the iliac crest due to friction of the loads over this site which bears the maximum weight.

It was unusual for the porters to be men of powerful build, and their average weight was 9 st. 10 lb. It is customary for the porters to work barefooted, and their feet are broad compared with a European's but singularly free from pes planum and hallux valgus.

Since the foundation of Iraq in 1921, many laws concerning the health and welfare of the working people have been passed, and today a new law has been drawn up with the help of a British adviser which will consolidate and bring up to date the already existing legislation. It is known as "The Law concerning Work and Workers" and does not cover agricultural workers. The clauses of this Bill have been compiled in keeping with the spirit of the age, and if carried out efficiently and conscientiously will place Iraq in the ranks of the most socially conscious nations.

(1) No child under the age of 12 years is to be employed and regulations are to be drawn up regarding the employment of young persons. (2) Pregnant women are to be granted three weeks' leave of absence on full pay before the date of their confinement and for three weeks after. (3) Nursing mothers are to be allowed two breaks of half an hour each in order to feed their children. (4) Articles are included to govern hours of work, night work, and overtime. (5) During Ramadan the daily hours are reduced by one. (6) A worker is entitled to annual leave on full pay at the rate of one day for each month worked. (7) Special provisions are set up to deal with claims for compensation, and there are schedules for diseases and rates of compensation. Permission is granted for the list of scheduled diseases to be amended as the occasion arises. (8) The formation of trade unions is legalized, and any employer who penalizes an employee for joining or not joining a trade-union is liable to punishment.

So far, the passage of this Bill through Parliament has been fairly smooth, and it is expected that it will be passed without any material alteration.

The subject of industrial health cannot be dismissed without some mention being made of the education of medical students in preventive and social medicine. The course in public health has been considerably modified to bring it more into line with modern concepts. Laboratory investigations into the analyses of water, milk, and food, have been replaced by outside visits and demonstrations, and an elementary course on the industrial diseases likely to be encountered in Iraq is included. As a symbol of this altered outlook, the Department of Public Health in the Royal Medical College is now designated as that of Public Health and Social Medicine.

Finally, a word must be said about the conditions of the handicapped worker. As in other countries of the Middle East the welfare of the disabled has been neglected, so that it is not unusual for such persons to drift into the ranks of the street beggars. There is a great need for this problem to be tackled in a radical manner: first, to introduce measures to prevent disabilities; secondly, to train handicapped persons in suitable employments; thirdly, to place them in industry, if necessary passing some enactment on the lines of the Disabled Persons Act in England.

Summary

Health conditions prevailing in the modern factories of Iraq are contrasted with those in the primitive workshops. A short description of the work and health of the porters of Baghdad is included.

My thanks are due to H.E. the Minister of Health, Iraq, for granting permission for publication.

BOOK REVIEWS

Dust is Dangerous. By C. N. Davies. (Pp. xvii + 116 ; illustrated. 21*s.* net.) London : Faber & Faber. 1954.

Here is an interesting book but not an easy one to fit into a category. According to the foreword and dust jacket the book should interest works managers and engineers and those concerned with occupational hygiene. On the other hand, much of it seems to be written rather as technical comment on scientific aspects of dust sampling and prevention. Many of the topics are not adequately introduced for the general reader : the works manager and the safety engineer will sometimes need to read between the lines if they are to understand the more complicated and occasionally diffuse sections of the text.

The first chapter of the book, on " Dust Hazards of the Industrial Worker ", forms an introduction of great general interest and is worthy of a wide public. It deals variously with the effects of widespread atmospheric pollution and with the many known hazards of special industrial dusts. The action of the ciliated epithelium in scavenging the lungs of dust particles is related in some detail and forms a suitable introduction to such topics as pneumoconiosis.

The illustrations of the first chapter are not always as well chosen as the topics of the text. Plate I shows a view of Donora in the United States where, in 1948, a disastrous chemical fog killed 20 people ; the scene is depicted in the fashion of those railway posters which succeed in giving romantic impressions of our more grimy industrial areas and is surely inappropriate. The illustrations of agricultural spraying machines add little that might not have been surmised from the legend alone. Plate III, of the " right and wrong way of filling a tank with toxic chemicals ", is of poor quality. A more effective means could surely be devised to illustrate protective clothing.

Chapter II forms a substantial part of the book and is very much Dr. Davies' own subject. To the initiated it will be regarded as an authoritative commentary on the sampling technology ; to others seeking only general enlightenment the sudden appearance of formulae and the rather deviously explained terms such as " isokinetic " will, perhaps, be a little frustrating. The chapter contains much of interest but in its concern to embrace so many methods and aspects of sampling it omits to give a clear recommendation to the reader as to which method might best be chosen in practice.

Chapter III deals at some length with preventive measures. This is a difficult field, for every problem needs a special solution of its own. The author gives an excellent account of the characteristics and limitations of the accepted combative measures. The survey shows, however, how far we still lack means that will, at no great cost and complexity, remove the smaller particles from the very large volumes of air commonly used in industrial processes.

Chapters V and VI collect together interesting and often elusive information on radioactive dusts and on household and non-industrial dusts. A final chapter on dust explosions outlines the principal features of this somewhat imprecise subject and shows how best to guard against some of the hazards.

As to the construction of the book as a whole, the reader is likely to be well satisfied. The standard of reproduction of the illustrations is generally high. The tables and indexes are attractively arranged and a very full set of references is included. The clarity might, however, be improved by the better introduction of the numerous special instruments and by the removal of jargon such as " kerf " and " cyclone ". Many errors or, at least, awkwardnesses of syntax should have been corrected. The explanatory script of the line diagrams is often tediously small. It should not have been necessary to leave on Figs. 8 and 9 the many spidery lines that call attention so obtrusively to the blocks' earlier existence in a different context. These faults are superficial and a future edition will, we hope, give an opportunity for correction.

R. A. Scott

Ätiologie und Prophylaxe des Lungenksebses (Aetiology and Prophylaxis of Lung Cancer). By F Lickint. (Pp. xv + 212 ; 29 illustrations. Price 21*s.* 6*d.*) Leipzig : Theodor Steinkopff. 1953.

A short survey of the distribution of lung cancer throughout the world and of its recent dramatic change in incidence leads Professor Lickint to the conclusion that the common squamous and undifferentiated cancers are preventable. The main part of the book is therefore devoted to an examination of the various factors—infective, chemical, and physical—which have been suggested as being of aetiological importance in these types of growth. Pride of place is given to tobacco but no possible industrial risk is overlooked. The author is not always as critical as he might be ; for example, he quotes Nordmann and Sorge's finding that 20% of animals exposed to asbestos dust developed squamous cell carcinoma without mentioning that the total number of animals involved was 10 and that other workers have

disagreed with the histological interpretation. But a book of this type is not likely to be used so much for its conclusions as for its references. For the latter it is invaluable, not only because of the number cited but also because of their catholicity. It is a pleasure to read a book in which full attention is paid to data coming from all countries. It is refreshing also to find an author who lays so much stress on the doctor's responsibility to apply his conclusions in the field of prophylaxis.

RICHARD DOLL

A Practical Manual of Diseases of the Chest. By Maurice Davidson. (Pp. x + 647; 255 figures. 84*s*.) Oxford University Press (London: Geoffrey Cumberlege). 1954.

A reviewer, with specialist knowledge in a limited field, is in a somewhat difficult position when reviewing a chapter on his speciality in a large textbook. It is impossible for textbooks, however frequently revised, to be completely up to date at the time of publication, and the problem is simply, "How out of date is good enough?", and, for a well known and widely respected textbook, it seems reasonable to expect it to be not more than two or three years behind the times.

Unfortunately, by this standard, the chapter on "The Pneumonconioses" must be severely criticized. The histogram (Fig. I) of the number of references related to date of publication tells the story quantitatively, and when the quality of the four most recent references are examined, three are found to refer to experimental animal pathology with very doubtful human applications, while the other refers only to the social problem of pneumoconiosis.

Although many of the old references have great value, it is impossible to neglect nearly all the work of the last 10 years without seriously misleading the reader. The reader should be told something of the work of Gough and Heppleston in differentiating the pathology of coalworkers' pneumoconiosis from that of silicosis. Similarly, the modern British radiological classification, which has been accepted as the international classification, should surely at least be mentioned. The author refers to the differences of opinion amongst doctors in interpreting *x*-ray films showing pneumoconiosis but makes no reference to the work of Fletcher in measuring this error and in reducing it by means of standard films. The medico-legal section too has an odd flavour. It must

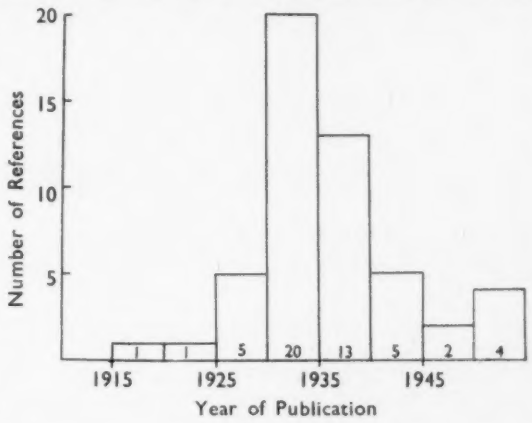

FIG. 1

antedate the National Insurance (Industrial Injuries) Act of 1946. The general effect is rather like a textbook on tuberculosis omitting the section on antibiotics.

However, a relative of mine once, to my horror, threw an expensive guide book to Scotland into the fire because it gave insufficient attention to the war memorial in Galashiels, so I would like to stress the probability of the excellence of the rest of the book, while advising readers to steer clear of the chapter on the pneumoconioses.

A. L. COCHRANE

Association of Industrial Medical Officers

In 1956 the Association of Industrial Medical Officers will celebrate its 21st anniversary by holding a meeting in London from September 24 to 29. The hosts will be the London Group of the Association, and the Scientific sessions will be held at the London School of Hygiene, which was the venue of the first meeting in September, 1935.

ABSTRACTS

(This section of the JOURNAL *is published in collaboration with the abstracting Journal,* Abstracts of World Medicine, *published by the British Medical Association. The abstracts are divided into the following sections : toxicology ; industrial physiology ; industrial lung disease ; industrial skin diseases ; accidents and orthopaedic surgery ; industrial ophthalmology ; environment ; general. Not all sections will necessarily be represented in any one issue)*

INDUSTRIAL TOXICOLOGY

Acute Carbon Monoxide Poisoning—an Analysis of One Hundred and Five Cases. MEIGS, J. W., and HUGHES, J. P. W. (1952). *Arch. industr. Hyg. occup. Med.*, **6**, 344.

A detailed analysis is presented of the records of 105 cases of acute poisoning with carbon monoxide admitted to the Grace–New Haven Community Hospital during the 29-year period 1920–48. The degree of poisoning was mild in 46 cases, moderate in 22, and severe in 37, 7 cases being fatal. No fewer than 98 of the patients showed signs of mental abnormality on admission. Of these, 74 were comatose or semi-comatose, the remainder disorientated, excited, depressed, or apprehensive. Lesions of the central nervous system occurred without apparent pattern, but the presence of incontinence (21 cases) was closely correlated with severity. The colour of the skin was more often cyanotic or flushed (71 cases) than pink or cherry-red (27 cases). Abnormal chest signs, mainly rales or rhonchi, were noted in 52 cases, being usually transitory and noted in different parts of the chest on successive days. Skin lesions developed in 31 patients, commonly an erythema resembling that of a burn. Some patients showed injection of the pharynx or suffusion of the conjunctivae. The heart rhythm was irregular in 18 cases. The findings on abdominal examination were recorded in 100 cases, in 23 of which the liver edge was palpable. Excessive sweating during the first 24 hours and occasionally recurring up to the 28th day was noted in 30 cases, localized pain and soreness in 20, localized oedema in 13, and a tendency to bleed in 11 cases. In 9 cases a remission of symptoms occurred between the 1st and the 4th days, followed by relapse between the 2nd and the 13th days. Of these patients, 4 died and 2 of those who recovered has serious permanent personality changes.

Clinically, these 105 cases could be divided into two groups : (1) In 68 cases poisoning was mild or moderate in degree and the clinical picture was of a rapid pulse, increase in blood pressure, irregular cardiac rhythm, suffusion of mucous membranes, localized oedema, tremor, headache, vomiting, increase in erythrocyte count, and slight glycosuria—signs suggesting disturbed function of the autonomic nervous sytem. (2) In 37 cases poisoning was more severe and the patients showed signs of injury to the central nervous system with associated stimulation of the pituitary-adrenal mechanism, changes in the colour of the skin, skin lesions, chest signs, tachypnoea (30 or more per minute), sweating, enlargement of the liver, localized oedema, tendency to bleed, rise of temperature to 102° F. (38·9° C.) or more, leucocytosis (18,000 or more cells per mm., with a decrease in the lymphocyte and eosinophil counts), albuminuria, and abnormalities in the urinary sediment. The presence of these signs together with those of Group 1 is of serious prognostic significance, all being present in the 7 fatal cases in this series.

M. A. Dobbin Crawford

Inhalation of Sulfuric Acid Mist by Human Subjects. AMDUR, M. O., SILVERMAN, L., and DRINKER, P. (1952). *Arch. industr. Hyg. occup. Med.*, **6**, 305.

Experiments were performed at Harvard University School of Public Health in which, for periods of 5 to 15 minutes, healthy adult volunteers inhaled sulphuric acid mist in concentrations varying from 0·35 mg. to 5·0 mg. per c. metre. Concentrations below the maximum allowable level of 1 mg. per c. metre were undetectable by odour, taste, or irritating effect, whereas a concentration of 3 mg. per c. metre was noted by all subjects, and 5 mg. per c. metre was objectionable, a deep breath causing cough. At all concentrations, however, pneumotachograph records showed that there was a quickening of respiration, breathing becoming shallower and expiration relatively prolonged. With a concentration of 0·4 mg. per c. metre the tidal volume in 5 subjects fell from about 900 ml. to 650 ml. after only 2 minutes' inhalation, and then remained constant until the end of the period of exposure. It then rapidly rose to about 1,090 ml. before returning to its initial level. At higher concentrations the type of response was the same, but it was more rapid and more marked and the return to normal was slower. Exposure to 0·5 mg. per c. metre for 5 minutes caused a marked reduction in minute volume in all cases, but the response was more varied in character since it was now no longer entirely reflex.

The mist particle size was found to average 1 μ and the average retention of inhaled acid was 77% for concentrations between 0·4 mg. and 1 mg. per c. metre.

Retention of the acid was found to decrease as the rate of respiration increased, and it is suggested that the more rapid, shallow breathing observed may be the result of a protective reflex mechanism.

Details are given of the experimental procedure and of the pneumotachograph tracings.

M. A. Dobbin Crawford

Tetraethyl Lead Poisoning. Report of a Non-fatal Case. WALKER, G., and BOYD, P. R. (1952). *Lancet*, **2**, 467.

The authors report in detail a typical case of tetraethyl lead (TEL) poisoning in a foreman who, for 3 years, had been employed in removing the TEL-containing sludge from storage tanks which had contained leaded petrol. The investigations carried out when the patient was admitted to hospital are described, special reference being made to the radiological demonstration of lead in the liver and to changes in the electroencephalogram. The routes of absorption of the TEL, the clinical picture, diagnosis, and treatment are discussed, and short notes on 5 other cases are given.

[This most interesting and lucid article serves to emphasize the importance of occupation as a factor in the differential diagnosis.] *A. Thelwall Jones*

Chronic Toxicity of Ammonia Fumes by Inhalation. WEATHERBY, J. H. (1952). *Proc. Soc. exp. Biol. (N.Y.)*, **81**, 300.

Exposure of male guinea-pigs to an atmospheric concentration of 170 p.p.m. of ammonia for periods of 6 hours per day, 5 days per week, for as long as 12 weeks gave no significant evidence of chronic intoxication. However, such exposure for 18 weeks resulted in relatively mild though definite changes in spleens, kidneys, suprarenal glands, and livers, with severity of the changes being most prominent in spleens and least in livers. Hearts, lungs, stomachs, and small intestines showed no consistent changes suggestive of chronic intoxication.—[Author's summary.]

INDUSTRIAL LUNG DISEASE

Criteria for the Evaluation of the Health Hazard in Dusty Occupations. PARMEGGIANI, L. (1953). *Med. d. Lavoro*, **44**, 65.

In this paper from the University of Milan the author discusses the criteria available for the evaluation of the risk of silicosis in dusty trades. Enquiries based on the present health of groups of employees give information on past exposure, but are of little value in estimating whether a risk is still present. Reliance must therefore be placed on physico-chemical methods of examination of dust; analysis of the materials from which dust is produced is not sufficient, as the dust may differ widely in composition from the material itself.

The relative value and uses of 15 methods of dust sampling are given. It is concluded that thermal and electrostatic precipitators give the best results in numerical counting of particles, the former particularly for particles of less than 5 μ. in diameter. For the quantitative determination of free silica by chemical methods, the Soxhlet filter paper and the salicylic-acid filter are recommended. Petrographic analysis is only of value where the particles are larger than 8 μ. in diameter; with small particles the *x*-ray diffraction method gives good results. The quantitative determination of free silica in any sample of industrial dust may be undertaken by the combination of *x*-ray diffraction analysis with chemical methods, preferably by fusion of the sample with potassium bisulphate and subsequent treatment with phosphoric and hydrofluoric acids.

The risk of contracting silicosis depends on many different factors which are summarized as follows: (1) objective factors, that is, nature of the material, or presence of free silica; (2) environmental factors; (3) the effectiveness of any methods of prevention in use such as local ventilation or respirators; (4) human factors, both collective and individual. The estimation of the silicosis risk in a working process must be based on the study of all these factors and must therefore be undertaken by experts in this field. Examples are quoted of various attempts which have been made to establish a maximum permissible dust concentration, but it is concluded that in the present state of our knowledge it is not possible to do so. Investigations are being continued by the U.S. Public Health Service, the Silikoseforschungsinstitut, Bochum, and the Clinica del Lavoro, Milan, and it is hoped to establish figures of maximum allowable dust concentrations for particular industries.

L. G. Norman

Pneumoconiosis due to Cement Dust. DOERR, W. (1952). *Virchows Arch.*, **322**, 397.

The author reports what he believes to be the first recorded case of severe pneumoconiosis attributable to the inhalation of cement dust—in a man of 47 who had worked for 25 years (1921–46) in the same Portland cement works near Heidelberg in very dusty occupations. There was no other history of exposure to dust. The condition was first detected in 1939 as the result of a routine *x*-ray examination, when nodular shadows in the lung fields were observed, but the man was fit and continued at work. In 1946 a radiograph showed massive shadows in the lung fields, and he became progressively more disabled and died in 1951. At necropsy massive fibrosis was found in both lungs, which contained numerous collagenous nodules interconnected by a fibrous reticulum. There was thickening of the pleura, and fibrosis in the regional lymph nodes. The massive fibrosis was collagenous, with hyaline connective tissue: it resembled silicotic fibrosis, but was of a somewhat looser texture and densely impregnated with cement dust. The blood vessels in the fibrotic areas showed endarteritic changes. There were deposits of cement dust in the liver and spleen. There was no evidence of tuberculosis.

The author then describes investigations carried out in an attempt to determine the aetiology of the fibrosis. Incinerated and acid-treated sections of the lung showed profuse dust deposits, the dust particles being, in general,

somewhat elongated, measuring up to 20 μ in length. Dust from the lungs and from the factory was examined mineralogically and by *x*-ray diffraction. The lung ash contained 50% total silica, which is a greater proportion than is commonly found in silicotic lungs. There was only 4% of calcium, compared with 40% in the parent dust, and the author considers that the calcium of the cement dust must have been dissolved away during life leaving a silicate residue behind. *X*-ray diffraction showed small quantities of quartz in the lung, but not in the parent cement dust, and also tracts of clay and mica. The author discusses the question of whether the fibrosis should be attributed to the predominant silicates so that the condition should be regarded as a silicatosis, or whether the disease is a " mixed-dust silicosis ". The presence of quartz in the lung might be accounted for by the presence of free silica in the parent material despite its apparent absence on analysis, or dust in earlier years might have contained quartz ; but the author dismisses these possibilities and concludes that the quartz must have arisen from the " weathering " of silicates in the lung in the course of time. He concludes that the condition must be regarded as a silicatosis (chiefly because of the character of the fibrosis) and that its development in this single case must be attributed to individual susceptibility on the part of the subject, coupled with excessive exposure over many years.

C. M. Fletcher

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It is suggested that the incidence of the condition is higher than may be apparent, as men were (for economic reasons) not always willing to volunteer for examination, and may be as high as 19% of all workers exposed, not including men with early symptoms. The gum acacia process is used only in colour printing, and the risk does not extend to those employed in black-and-white printing. Efficient ventilation will mitigate the hazard, but it can be eradicated only by the substitution of dextrose for gum acacia in the spray fluid, as suggested by Bohner.

L. W. Hale

INDUSTRIAL SKIN DISEASE

Interdigital Sinuses of Barbers' Hands. CURRIE, A. R., GIBSON, T., and GOODALL, A. L. (1953). *Brit. J. Surg.*, **41**, 278.

The authors review an occupational condition which is more prevalent than is usually realized, since the patient seldom seeks medical advice—namely the interdigital sinuses which occur on barbers' hands. At the Glasgow Royal Infirmary they examined the hands of 77 gentlemen's hairdressers, in 10 of whom some stage of interdigital sinus formation was present ; the hands of none of 61 ladies' hairdressers showed any similar lesion. Only 18 cases have previously been recorded, and clinical details of these and of the present authors' 11 cases are tabulated.

The condition is characterized by pits and sinuses on the webs of the fingers which occur most commonly between the fore and middle fingers or middle and ring fingers of the right (cutting) hand. These are due to penetration of the skin by the short, sharp hairs which accumulate between the barbers' fingers, followed by secondary infection and granuloma formation. The mechanism whereby the hairs penetrate to the corium and even to the subcutaneous tissue is discussed. The sinuses are all lined by squamous epithelium, and the microscopical appearances of the various types of sinus are described and beautifully illustrated. Brief mention is made of other hair-bearing lesions, including scarring pseudo-folliculitis of the negro beard, postanal pilonidal sinus, and similar sinuses which have been described in the perineum, axilla, umbilicus, sole of the foot, and suprapubic area, and a plea is made for a more accurate nomenclature.

Simple prophylatic measures would prevent this condition altogether. Once developed, it is an irritating disability which may require surgical excision of a deeply situated granuloma, sometimes followed by skin-grafting.

John Huston

Hop Dermatitis in Herefordshire. COOKSON, J. S., and LAWTON, A. (1953). *Brit. med. J.*, **2**, 376.

An investigation of the incidence of hop dermatitis among workers in the hop-yards in Herefordshire in 1952 revealed that one in every 30 pickers had a mild form of dermatitis. Severe dermatitis was, however, rare, and was associated with oedema of the face and hands and exposed parts. The incidence of this severe form was probably no higher than 1 in 3,000 pickers.

In some cases the dermatitis appeared to be due to a sensitizing ingredient of the hop-oil, which, however, was lost in the process of drying, thus accounting for the rarity of hop dermatitis among workers in dried hops. In some cases a positive reaction to hop resin was obtained.

John T. Ingram

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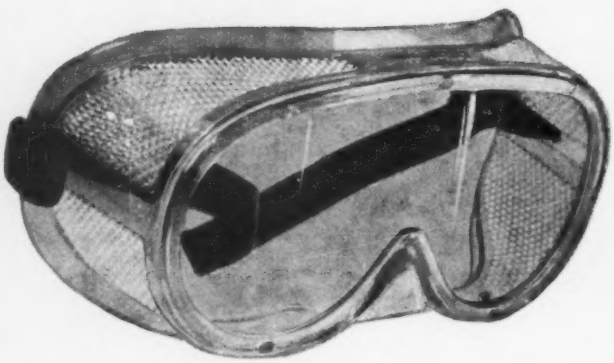

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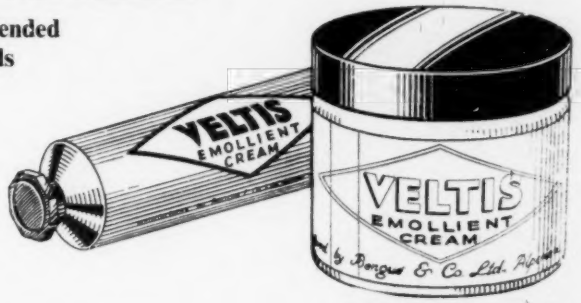

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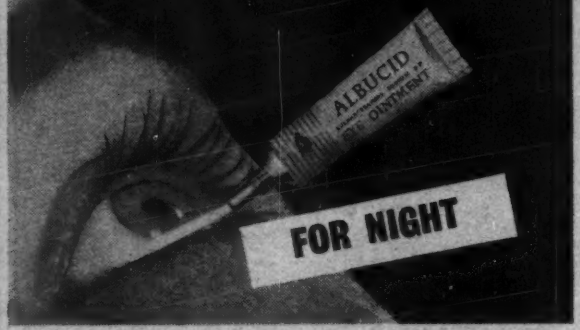

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